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Ethical Dimension of Consuming Frog Components for Medical and Research Purposes

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Abstract
Amphibians are known to possess a moist integumentary system which plays a vital role in its cutaneous respiration. In addition to this, its skin also possesses granular and mucus glands which secrete several potent bioactive compounds that enable them to protect themselves against predators and microbial infection. Recent development in technology have made it possible to extract certain compounds from amphibians which harboured a specific bioactivity characteristics such as antiviral, antibacterial, antifungal, antiprotozoal, antidiabetic, antineoplastic, analgesic and sleep inducing properties. Amphibian biology has provided us with an insight that could help mankind in treating various illness. Their immune defences are highly evolved by both innate and adaptive immune system. Therefore, this paper aims to discuss and elaborate on how Islam jurisdiction affects the rulings of frog components use for medical and research purposes.

Keyword: *Frog components, medication, Fiqh opinions*

Abstrak
Amfibia dikenali mempunyai sistem integumen yang lembap yang memainkan peranan penting dalam pernafasan kulit. Di samping itu, kulitnya juga mempunyai kelenjar bergranul dan berlendir yang merembeskan beberapa sebatian bioaktif poten yang melindungi diri daripada pemangsa dan jangkitan mikrob. Perkembangan terkini dalam teknologi telah memungkinkan untuk mengekstrakkan sebatian tertentu dari amfibia yang mengandungi ciri-ciri bioaktiviti tertentu seperti antiviral, antibakteria, antifungal, antiprotozoal, antidiabetic, antineoplastic, analgesik dan sifat mencetus tidur. Biologi amfibia telah memberikan idea yang dapat membantu manusia dalam merawat pelbagai penyakit. Pertahanan imun berevolusi secara semula jadi dan adaptif oleh sistem keimunan. Oleh itu, kajian ini bertujuan untuk membincangkan dan menghuraikan bagaimana bidang kuasa Islam mempengaruhi keputusan komponen katak yang digunakan untuk tujuan perubatan dan penyelidikan.

Kata kunci: *Komponen katak, Perubatan, Pandangan Fi'qah*

Introduction

Herpetology can be defined as a study of amphibians and reptiles, which is one of the branches in zoological studies. This field involves herpetofauna which consist of amphibians including frogs, toads, salamander, newts and gymnophionae and reptiles (including snake, lizard, amphisbaenids, turtle, terrapins, crocodilians, and the tuataras). Frogs are amphibians in the order Anura. Their distinctive features include: no tail, a short, often stocky body, long hind legs and short front ones, large bulging eyes, and a very wide mouth (Inger & Stuebing, 2005). Amphibian skin is overly exposed to different environmental conditions such as dryness and moisture. Such conditions have allowed them to interact directly with other environmental factors such as microorganisms, parasites, predators and also physical factors. Therefore, they provide a valuable information about prospective functional molecule. Over the past several decades, bioactive compounds of amphibian skin secretions, especially biologically active peptides, have been extensively studied (Bevins & Zasloff, 1990; Li et al., 2008; Li et al., 2007; Ma et al., 2010; You et al., 2009).

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Biological activity of amphibian secretions

In general, on the basis of structural similarity, amphibian skin possesses four types of glands that secretes specific compounds which are granular glands for poison and bioactive peptides, mucous gland for skin lubrication, mixed gland for both function and lipid or wax gland (Brizzi, 2001). As mentioned earlier, amphibian secretions possess numerous biological activity. Research has proven that secretions from amphibian are known to inhibit the growth of microbial organism such as bacteria, viruses and fungus (Jenssen, Hamill, & Hancock, 2006). The effectiveness of bioactive peptides in amphibian secretions became less potent when tested against Gram-negative and Gram-positive bacteria such as *Staphylococcus aureus, Sarcina lutea, Enterobactacter aerogenes, Candida albicans, Bacillus cereus, Bacillus subtilis, Escherichia coli, Proteus vulgaris,* and *Salmonella typhimurium* respectively (Afsar & Kalyoncu, 2011). These results indicate that despite living in a unpredictable weather and harsh environment such as environment with high or low in pH, salinity, and water with high in biological oxygen demand (BOD) (Obilonu, Chijioke, Igwegbe, Ibearugbulem, & Abubakar, 2013), the amphibian itself is able to defend itself against pathogenic bacteria which could in turn, provide an insight for the benefits of a mankind. The secretions do not just actively inhibit the growth of bacteria, but also fungus. Toad secretions were taken as an objective to inhibit the growth of fungus strains such as *Rhodotorula rubra* and *Saccharomyces cerevisiae.* The secretions were proven to show a high a potent activity against both species of yeast cultures (Dülger, Ugurtas, & Sevinc, 2004).

In medical field, the emergence of multi-drug resistant organisms such as methicillin-resistant *S. aureus* (MRSA) have stirred a massive concern across medical practitioners. Therefore, this leads to various scientific exploration that could help in fighting the issues. Since the efficacy of amphibian secretions have been proven in numerous researches against numerous microorganisms, it is postulated that the antimicrobial peptides which are present in the amphibian secretions are the basis of overall effectiveness of their biological activity. Naturally, the antimicrobial peptides sizes occur at less than 10kDa with an overall net positive charge, hydrophobic and membrane active. The secondary structure of these molecules follow four different themes namely α-helical, β-pleated sheets or stranded due to the presence of two or more disulphide bonds, β-hairpin or loop due to the presence of single disulphide bond or cyclization of the peptide chain and lastly, the extended form of the structure (Dhople, Krukemeyer, & Ramamoorthy, 2006). AMP with a C-terminally α-*amidated* structure contributes to the higher potency when tested against MRSA (Conlon & Mechkarska, 2014). Such structures are also reported as having to be highly conserved and diversified within species or families (Conlon, 2011) and the variation of its secretions contain different peptides with broad-spectrum of antibacterial and antifungal activities and also the ability of them to permeabilize mammalian cells (Conlon, Ahmed, & Condamine, 2009). Nevertheless, previous literatures on AMP derived from animals and its bioactivity have been reviewed (Zasloff, 2002).

Other than bacteria and fungus, the secretions also showed a promising candidate in fighting off viral replication and infection. Rabies is a type of zoonotic disease which could lead to fatality and often neglected in more than 150 countries. It is caused by a single strand RNA which affects human's central nervous system through an infection initiated by the muscular nicotinic acetylcholine receptor. A person infected with rabies virus may feel similar to flu but with a prickling sensation at the bite area and progressing within days until signs of cerebral dysfunction, anxiety, confusion and agitation. A compound isolated from toad species have provided the exhibit in which the compound, bufotenine, successfully prevent the penetration of the single stranded RNA of the virus (Vigerelli et al., 2014). The cytotoxic tests were performed over baby hamster kidney (BHK-21) using MTT test. In the experiment, rabies virus strain Pasteur vaccine (PV) was used on fluorescence inhibition test and fluorescent foci inhibition test, with both done simultaneously and time course treatment of the cells with the virus and bufotenine. The results in the experiment are significant in at least two major aspects that is the bufotenine itself can inhibit the penetration of rabies virus in mammalian cells through an apparent competitive mechanism by the nicotine acetylcholine receptor. It is also known to take action in dose-and-time dependent manner which pointing out to a specific mechanism of action.

As the research progressed, researchers have been able to identify and widen the scope of its biological activity through various biological assay. The cutaneous secretions of amphibians have been reported to have a significant killing activity when tested against etiological agents of Visceral Leishmaniasis, Chagas disease and Toxoplasmosis (Gustavo Tempone et al., 2007). This finding involves the subject of eight anurans but only one presented antileishmanial activity against the extracellular promastigotes of *Leishmania chagasi*, with an IC_{50} of 248.8 µg/ml. Meanwhile, four other anuran skin

secretions showed promising antitrypanosomal activities as they presented a significant killing activity, especially when a pool of compounds in crude extracts, with IC_{50} values ranging from 32 to 143 µg/ml is considered. Last but not least, further studies on antiprotozoan activity of the secretions against *Trypanosoma cruzi* have been reported to show a significant killing effect as no protozoan cells were detected at the end of the experiment (Brand et al., 2002). Anti-protozoan activity in the literature was investigated using *Trypanosoma cruzi* in its trypomatigote and epimastigote forms cultivated in both cell culture and blood media. After two hours of incubation with DS 01 at a final concentration of 6 µM, no protozoan cells were detected.

Table 1: Peptide representative of amphibian origin

	Representative peptides	Origin	Tissue
Magainin 2	GIGKFLHSAKKFGKAFVGEIMNS	Frog	E
Dermaseptin 1	ALWKTMLKKLGTMALHAGKAALGAAADTISQGTQ	Frog	E
Brevinin 1T	VNPIILGVLPKVCLITKKC	Frog	E
Buforin 2	TRSSRAGLQFPVGRVHRLLRK	Vertebrate	E
Ranalexin	FLGGLIKIVPAMICAVTKKC	Frog	E

*E = epithelial tissue

Understanding of amphibians from Islamic perspective

In order to have a better understanding on the status of amphibians from Islamic perspective, various sources have been reviewed and taken into consideration. It is important to know that in Islam, the animals have been divided into three categories which is aquatic animals, terrestrial animals and amphibious animals (Al-Zuhayli, 2007). Amphibians are known to possess a moist skin and can live both on land and in water such as frogs, toads, salamander and newts. Such characteristics have enabled scholars to have a different opinions in order to determine the ruling that is applicable to this type of animal, particularly amphibians.

Halal and Haram does not stand for an act of convict alone, but also the consumption of food and status of living things, with regards to *Qur'an*, *hadith*, *Ijma'* and *Qias*. In the Islamic law or Shariah, there are different categories of animals with regards to the opinion of Muslim scholars. According to Al-Zuhayli (2007), there are two ways of categorizing animals, namely aquatic animals and terrestrial animals. In his opinion, aquatic animals are those animals that makes water as their primary habitat.

Certainly, the rulings on such matter is affected as how one's perceived the notion of amphibians. In Islam, the rules of prohibition and permissibility is derived from the *Qur'an* and *hadith*. For instance, *Qur'an* and *hadith* are the relevant sources to be referred to in case of any questionable issues or unclear principle. It is appropriate to say that there is no clear or direct statements in the *Qur'an* which actually mentioned on the ruling of amphibians as if it were to be consumed as a part of human's diet or as a source of therapeutics medications. In the process of establishing the given ruling, which is apart from *Ijma'*, there are few other factors that are taken into consideration especially custom or *adah*. This is because as stated in the jurisprudential maxim, in some cases, custom is the basis of rulings. *Adah* literally means custom and in this context, it means the general practices of a given society which is accepted as part of their daily life (Al-Zarqa, 1969). The Prophet Muhammad S.A.W had declined the offer of dining on the *dhobb* but he neither permitted it to be consumed by others nor mentioned it is haram but rather it was not his usual diet back in his land. This could lead to an example of having frogs to be consumed as mentioned in Mazhab Maliki which allows frogs to be consumed due to no mentioned authority or *nas.* Therefore, it cannot be concluded as *al-khabaith* (Abdullah Ibn Abbas, n.d.) which means impurities.

The differences in how each school of thought perceived this issue have come to the terms that there are no strict or direct rulings from the *Qur'an* that mentioned the impermissibility of the consumption of amphibians or amphibian products and thus creating a difference in *fatwa*. Therefore, the sole focus of this topic is to discuss and distinguish the opinions of different school of thoughts on amphibians.

Fiqh Ruling of amphibians

Scientific evidences have proven the effectiveness of amphibian secretions when tested against various types of microbial pathogens in vivo. It can be said that amphibians have been consumed as part of medications all over the world especially as a traditional Chinese medicine, chan su in which it is

used to treat heart diseases and various systemic illnesses (Bhuiyan, Fant, & Dasgupta, 2003). Generally, animals that are classified as halal or haram for consumption is based on the clear evidences from the *Qur'an* and the permissibility and prohibition that has been explained by the Prophet himself (Mahyeddin, Mustafa'Afifi, & Nazmi, 2013). Due to this, the Muslim jurists appeared to be very cautious in providing such fatwas and it is achieved through the process called ijtihad. Ijtihad means the effort made by the jurist in order to master and apply the fundamental rules of legal theory which aims to discover God's law (Hallaq, 1984).

Table 2: The justifications of different madhab regarding amphibians

School of thoughts	Justification	Reference
Hanafi	*Haram* for consumption because it was decided as *al-khabaith* and the presence of toxins or venom in some species affected its rulings.	(Al-Zuhayli, 2007)
Shafie'	*Haram* for consumption because it was decided as *al-khabaith* and the presence of toxins or venom in some species affected its rulings	
Maliki	It is acceptable and allowable to eat small vertebrates and invertebrates such as insects because there is no direct rulings on its prohibition which resulted in not belonging to the *al-khabaith* category	
Hanabilah	Animals that live in both aquatic habitat and terrestrial habitat are *haram* except if the animal are being slaughtered. In addition to this, according to the opinion of Imam Ahmad, animals without blood flow, such as crabs are halal for consumption despite without being slaughtered. However, the scholars also have prohibited the eating of frogs and crocodiles	

Recently, the Egypt's Highest Fatwa Council (2014) produced the fatwa about frogs. It specifically bans the killing and consumption of any frogs as the ruling were made based on the *hadith* narrated by Ibn 'Amr who mentioned that a frog's croaking is a praised to Allah S.W.T. On the other hand, the fatwa's produced by Religious Council of Brunei Darussalam (2010) mentioned that even though frogs are forbidden to be killed, an exception has been made to certain amendments in which it stated that any product derived from live land animals except pigs and animals with fangs and tusks that are halal can be used as a starting material for medicine. In terms of understanding, it is permissible for amphibians to be used as a starting material since there is no direct rulings of its permissibility status in the *Qur'an* itself.

The matter of discussion regarding this issue alone is not limited to a certain country only as it is debatable and still open for opinions. It is believed that the consumption and utilization of amphibians particularly frogs has becoming a norm in culture across countries. For instance, Majlis Ugama Indonesia (1984) has decreed a fatwa based on different points of view regarding the usage and consumption of frogs. The arguments that were addressed in the council were pretty much indifferent among others but with an additional points of agreement. It was decided that all living animals are not *najis* except dogs and pigs. In addition to the mentioned fatwa given by Majlis Ugama Indonesia (1984), it was recognized that certain species of frogs are considered halal for consumption as it does not bring harm to the mankind.

As for fatwa disclosed by Jabatan Kemajuan Islam Malaysia (JAKIM), the consumption and breeding of frogs is merely haram due to its biological behaviour which inhabits both on land and water. JAKIM produced the ruling based on the *Shafi'e'* sect which mentioned that every living animals that live both on land and in water are *haram* for consumption.

Conclusion

As a conclusion, the evident have shown that there are bound to be some ethical issues regarding the status of the amphibians itself if it were to be made into a source of medication. It is, indeed true, that some schools of thought have viewed that the consumption or utilization of amphibians, particularly frogs and toads are somewhat haram and are not permissible at all and reasons given for such forbidden practice were

based on the *ahadith* narrated by different people. However, no specific ruling had been made on the status of amphibians in the *Qur'an* and this is probably why only one mazhab allows the consumption or utilization of frogs. This results on the issue is open for questioning and debatable among modern Muslim scientist and jurists.

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