Zootherapeutics (Animal-based remedies) for urolithiasis: History, current scenario and future dimensions

Salman Ahmed, Maaz Uddin Ahmed Siddiqui, Imran Ahsan Mallick and Muhammad Mohtasheemul Hasan

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Abstract
Animals like plants are also medicinal agents for the prevention and cure of different health problems all over the world practically in about all human cultures. The concept of zootherapy is very old and has strong evidence of the medicinal use of animal resources. Different animals, their parts and derivative products are used and this is a heritage that could constitute a fundamental step for the discovery and isolation of natural extracts and new and low-cost alternative drugs from animals. About 12% of people in the world are affected by different types of urolithiasis and the recurrence rate in female is 47-60% and in male is 70-80%. According to WHO 75% population rely on traditional medicines for the prevention and cure of different diseases. Hence there is a need to concentrate on all folk natural products effective in urolithiasis for their pharmacological evaluation, isolation of single drug molecule responsible for anti-urolithiatic activity to developed suitable formulations used against urolithiasis.

Keywords: Zootherapy, urolithiasis, Ibn Sina, Al-Antaki

Introduction
Natural resources (plants, animals, minerals and microbes) are the richest source of medicinal agents based on the belief and observations regarding their folk and traditional uses for the prevention and cure of different diseases. A large number of research findings and the data are utilized by the scientific community in evaluating and establishing the pharmacological activities of these natural resources. Healing with animal parts or products is called Zootherapy. Animal based therapeutic agents are usually obtained from the animal body parts, metabolic products and other bodily secretions as well as non-animal materials such as nests and cocoons etc. Zootherapy is very popular among ancient cultures throughout the world [1].

Historical evidences of Zootherapy
Using animals as a medicinal agent is reported throughout the history [2]. Snakes have been considered as a sign of medicine and healing both by virtue of its associations with God of Medicine (Asclepius) and God of Health (Hygeia) in Greek mythology (B.C. 2000-400) [3]. Discussing the historical evidences of Zootherapy, Ebers Papyrus (written around 1550 B.C.) contain medicinal uses of birds, beasts, insects, reptiles, fish, eggs, milk, etc. and excrements of living animals blood, flesh, bones, fat, marrow and hide of carcasses, the shell of the tortoise, feathers of birds, the slough of snakes and the quills of the porcupine, entire body of insects and worms, brain, eyes, feet, gall, hair, head, heart, hoofs, horns, jawbone, legs, liver, spleen, teeth, testicles, uterus and vulva of ordinary animals were used as medicine. Grease or fat of the goose and ox were employed in a large number of medical recipes.
Ancient mesopotamia, mainly the Assyrian and the Babylonian texts contain medicinal use of fish oil, honey and bee wax, turtle shell, mongoose blood, skin of goat, sheep and deer, bird excrement and animal fat. Compendium of Materia Medica written by Li Shizhen in 1578 A.D. contain the medicinal use of bear gallbladder and bear fat as a medicine. Ancient Ayurvedic literatures, Sharaka Samhita (900 B.C.), contains 380 and Sushruta Samhita (600 B.C.) described 57 drugs of animal origin as therapeutic agents such as honey, milk and its derivatives, bones, bone marrow, fat, bile, blood, faces, flesh, urine, semen, skin, ligaments, shell, feathers and horn. Dioscorides in De Materia Medica book II mentioned zootherapeutics domestic animals, fishes, birds, insects and products of larger animals such as butter, milk, cheese, wool, fat, wax, marrow, blood, gall and the excrements. The entire body of cantharid beetles, grubs, earthworms, millipedes, cockroaches were crushed, dried, burned or cooked and applied in the form of a powder, salve, poultice; cockroaches are ground up in an oil and used for ear ache. Similarly millipedes are taken internally with wine and for kidney trouble and epilepsy [2].

Zoo-therapeutic is based on indigenous knowledge system built up by a group of people through generations, by living in close contact with the nature and use of traditional drugs of animal origin in the local environment so that it is specifically adapted to the local people and conditions. This plays an important role in the healing practices, of both indigenous and western societies throughout the world [4]. Not only the ancient systems but also the modern medical system utilizes animal based medicines [1]. In modern world, zootherapy is an important alternative mode of therapy among many other known therapies practiced in different parts of the world. Domestic and wild animals and also their by-products (e.g., bones, skins, hooves, feathers) are important ingredients in the preparation of protective, preventive and curative medicines. In Traditional Chinese Medicine (TCM), more than 1500 animal species are listed for different medicinal uses. While in India about 15–20% of the Ayurvedic medicine is based on animal and animal-derived substances [5]. There is a strong connection between medical ethnozoology of ancient and modern times as the combination of bull’s bile and honey, a classical Hippocratic remedy for intestinal constipation, remains functional till today [2].

The study of local or traditional zoological knowledge offers not only the possibility of new insights into biological phenomena, but also the opportunity to cross-check scientific hypotheses. Unfortunately, the traditional and historical knowledge has been historically pushed aside by the scientific community but now its importance has now being recognized by scientists and researchers and they are intensifying research on this theme [6].

Despite their importance, studies on the medicinal utilization of animals body parts and products have been neglected, when compared with plants. The use of animals and their products as therapeutic agent is not simply a matter of the pharmaceutical and medical sciences and therefore joint-research programmes should be undertaken with the experts of ecology, linguistics, anthropology, sociology, etc. Thus, discussing zootherapy within the multidimensionality of sustainable development turns out to be one the key elements in achieving the sustenance of medicinal faunistic resources [9]. Therefore, it is essential to document all the zootherapeutic uses and develop conservation strategies for animals before these traditional and indigenous beliefs, customs, values, know-how and practices are changed and rendered unsuitable, making the knowledge base incomplete [4].

Animal substances are not as numerous as those of plant substances but have played and continue to do so an important role in the prevention and cure of diseases. In fact, various animals prescribed in the past are still in use as recommended either for the same problem as originally described or for distinct conditions in traditional medicines used in different regions. Increased in knowledge and understanding of the medical systems in a historical context can potentially bring new insights into the medical significance of fauna in the past, as well as open new therapeutic perspectives in the future. The historic and sustained use of naturally occurring substances often has a scientific underpinning and the persistence of utilization of animal resources may indicate the presence of biologically active compounds [2].

Urolithiasis is derived from two Greek words ouron meaning urine and lithos stone. It is commonly considered as stone formation in any part (kidneys, ureters, urinary bladder and urethra) of the urinary tract. It is one of the oldest, most frequent and highly recurrent disorder and as reported was initially found in the tombs of Egyptian mummies dating back to 4000 BC [7]. At the initial stage, the stones are usually as small as a grain of sand and may gradually increase in size as large as a pearl or even a golf ball. These stones get stuck in the urinary tract causing urinary tract obstruction with hematuria, dysuria, nausea and vomiting. Peoples are at the risk for stone recurrence if they have stone before or any family history of urolithiasis. The other risk factors are not drinking enough water, diet rich in protein, sugar and sodium, being obese or experiencing gastric bypass surgery [8, 9]. The information provided in this review is obtained from Google Scholar, Pubmed, Sci Finder, Scirus, Web of Science and a library search. The search terms are included Ethnomedical survey of anti-urolithic animals, zootherapy against kidney stones, traditional zoo remedies for urinary stones. During this search, we found animal drugs mentioned by Ibn Sina in Al Qanoon Fit Tibb and Al-Antaki in Tadhkirat Uli l-al-Bab-wa l-Jami li-l-Ajab Al-‘Ujab successfully used against urinary stones in those times (Table-1). Ethnomedical surveys from Albania, Brazil, China, India, Jordan, Lebanon, Peru, Spain, Syria, Tibet, Turkey revealed the current use of animals against urinary stones (Table-2).

Table 1: Animal drugs mentioned by Ibn Sina and Al-Antaki in their well-known books for urolithiasis management

| Scientific name | Common name | Parts used | Mode of use (Orally taken) |
|----------------|-------------|------------|---------------------------|
| Androctonus crassicauda Oliver. | Arabian fat-tailed scorpion | Whole body | Ash of whole scorpion dissolves and expels urinary stones. |
| Erinaceus europaeus L. | Hedgehog | Spines | Ash of spines with Frankincense expels urinary stones. |
| Equus hemionus Pallas. | Asian wild ass | Urine | Urine dissolves urinary stones. |
| Gallus gallus domesticus L. | Hen | Egg shell | Ash of hen egg shell dissolves and expels urinary stones. |
| Lumbricus terrestris L. | Earth worm | Whole body | Whole earth worm taken with Frankincense expel urinary stones. |
| Mus musculus L. | Mouse | Stool | Ash of mouse stool dissolves and expels urinary stones. |
| Oryctolagus cuniculus L. | Rabbit | Whole body | Ash of whole rabbit dissolves and expels urinary stones. |
Urolithiasis: an overview.

From past to present: Medicinal zootherapy used against urinary stones prevention and treatment.

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Table 2: Zootherapy used against urinary stones in different countries and cultures

| Scientific name                  | Common name       | Parts used                  | Country            | Administered orally                     |
|----------------------------------|-------------------|-----------------------------|--------------------|----------------------------------------|
| Capra hircus L.                  | Goat              | Horn, legs and hoof         | Syria, Lebanon, and Jordan | Ash of body parts (Horn, legs and hoof) break up urinary stones [12] |
| Gallus gallus L.                 | Hen               | Gizzard                     | Albania, China     | The membrane of the muscular stomach (Mulitis puke) of a hen is removed and dried, then ground and made into a decoction intake to pass urinary stones [13, 14] |
| Himalayapotamon atkinsonianum Wood-Mason. | Freshwater crab | Flesh                       | Tibet              | To pass urinary stone; the gizzard is removed, washed, dried and pounded, then eaten [15] |
| Hippocampus gutulatus Cuvier.    | Long-snouted seahorse | Whole body                 | Spain              | Crushed with thorns and eaten or drunk in wine [17] |
| Lambricus terrestris L.          | Earth worm        |                             | India              | Earth worm baked with bread expels urinary stones [18] |
| Merlangius merlangus L.          | Whiting or merling fish | Otoliths (fish ear stone)   | Spain              | Swallow with water [17] |
| Periplaneta americana L.         | American cockroach | Whole body                  | India              | Ash of American cockroach in crude liquor dissolves urinary stones [19] |
| Plagioscion squamosissimus Heckel. | South American silver croaker/Corvina (fish) | Otoliths | Brazil              | Swallow with water dissolves urinary stones [19] |
| Pteropus vampyrus L.             | Flying fox (the world largest bats) | Urine                     | India              | Rice soaked in bat urine, dried and orally taken [21] |
| Petaurista petaurista Pallas.    | Giant flying (Squirrel) | Bile                       | India              | Bile is collected in bottle and drink with water [20] |
| Uppa epops L.                    | Eurasian hoopoe   | Flesh                       | India              | Boiled or cooked flesh is orally taken [20] |
|Apis mellifera L.                 | Propolis          | Bee glue                    | Peru               | Drinking of 15 drops of Propolis tincture (one part of propolis, and 10 parts of vodka or alcohol) for 2 weeks expels or flush out urinary stones [21, 22] |

Future dimensions

The understandings of the pathophysiology of urolithiasis and the mechanism of action of animal based agents are of great importance for the development of safe and effective anti-urolithiatic medicines. At present, known plant medicines have shown their anti-urolithiatic effect with multidimensional pharmacological actions as antioxidant, analgesic, anti-inflammatory, astringent, antispasmodic, Angiotensin converting enzyme inhibition, crystallization inhibition, demulcent, diuretic, litholytic, lithotriptic, Phospholipase A2 inhibition and also by changing the ions concentrations in urine such as increase magnesium and citrate excretion [23]. As a future dimension, it may be said that by using the available data in different in vitro and in vivo studies are required to find out the actual mechanism of the reported zoo therapies against urinary stones prevention and treatment.

Conclusion

This review concerning the Zootherapy reveals that humans have always considered animals as a source of surprising and numerous therapeutic properties. A high diversity of animal parts and derivative products are used and this is a heritage that could constitute a fundamental step for the discovery and isolation of natural extracts from animals in the search for new, safe, more effective and low-cost drugs. Likewise, the data documented also invite further research to determine the validity of these folk remedies.
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