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Empirical evidence of animals used in biomedical research in unani medicine: An appraisal

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Abstract
The Unani system of medicine is principally based on humoural theory which was propounded by Hippocrates. According to this theory, health and disease depends on the equilibrium of four humours i.e. blood, phlegm, yellow bile and black bile. From the ancient times, experiment on animals has been part of research for so many discoveries in Unani system of medicine. The notable ancient Unani physicians such as Aristotle and Erasustratus have dissected animals for the study of anatomy and physiology of various organs. Both of them have been considered as pioneers of anatomy in medical science. The most notable ancient Unani physician Galen has also performed vivisections. He did experiment on roosters to evaluate the efficacy and safety of one of the most commonly used antidote i.e. *tiryaq.* Ibn al-Nafis described blood circulation in mammals. Razi had tested toxicity of mercury in monkeys. Ibn Zuhr, a most versatile physician had developed some surgical procedures in animals before applying them on human being. Presently, animals are integrally being used for the evaluation of safety and efficacy of drugs. The antiarrythmic property of *Ajamline* has been first tested in animals. Likewise, cardioprotective effect of *Khamira abresham Hakim Arshad Wala* has been evaluated in isoproterenol-induced myocardial necrosis in rats. All these studies amply prove that preclinical studies are also part of biomedical research in Unani medicine since its inception.

Keywords: experimental animals; biomedical research; unani medicine; evidence based medicine

Introduction
The Unani system of medicine was basically originated in Greece and has subsequently been developed by Roman, Arabic, Spanish, Iranian and Indian physicians. Since then this system of medicine is also known as Greco-Arab Medicine. The Unani Medicine has been transformed into medical science based on the frame work of the teachings of Buqrat (Hippocrates, 460-370 BC) and Jalinus (Galen, 129-210 AD). It is primarily based on Hippocratic doctrine of four humours viz. *dam* (blood), *balgham* (phlegm), *safra* (yellow bile) and *sauda* (black bile) with their four temperamental qualities respectively viz. hot and moist, cold and moist, hot and dry, & cold and dry. According to Unani principle, the human body is composed of seven basic principles viz. *arkan* (element), *mizaj* (temperament), *akhlat* (humours), *a'aza* (organ), *arwah* (pneuma), *quwa* (faculties) and *afa'l* (functions). The mere absence of any of the component threatens the very existence of life and derangement of which results in disease. Hence, the main aim of a Unani physician is to restore the balance primarily by aiding bodily Faculties viz. *tabiate mudabbir-e-badan* (medicatrix naturae). The Unani system of medicine is still prevalent and practiced in many countries including India where the Conventional medicine still holds the sway [1].

In Unani Medicine, almost all the single as well as compound drugs have been tested directly on human being rather than on animals in ancient times. Ibn Sina (Avicenna, 980-1037 AD), one of the most critic on drug testing in animals, has depicted a whole chapter in the second volume of '*Al-Qanoon fit Tib*' (Alcanon) on testing of simple drugs. He stated that *"the potency of drugs' nature (amzija) can be identified in two ways; one of them is analogy (qayas) and another one is by way of experimentation (tajrubah). So, we say that experimentation leads to confident knowledge of the potency of drugs"*. Ibn Sina further specified seven rules which should be taken into consideration while performing testing of a new medicinal substance. He discussed in details about the importance of each prerequisite which should be aware by physicians. The guideline for testing of new medicinal substance which was given by Petrus Hispanus and St. Amand in 13th century AD was much similar to the guideline which was mentioned by Ibn Sina [2]. Ibn Sina opposed drug testing in animals because the temperament of human and animals are quite different. He insisted that a new medicinal substance should be tested in human being directly [3].

However, some ancient Unani physicians have tested certain drugs on animals to evaluate the safety and efficacy. Some ancient Unani physicians have also dissected animals for the study on anatomy, physiology, pathology and for other purposes [4].

Vivisection

The earliest evidence of experimentation on animals has been recorded since ancient times. Arastu (Aristotle, 384–322 BCE) and Erasistratus (304–258 BCE) were the two first Greek scholars who performed experiments on animals [5]. They carried out vivisections on animals to describe anatomy and physiology of various organs [6]. Jalinus dissected pigs and goats and considered as the "Father of Vivisection". Abu-Marwan Abdel-Malik Ibn Zuhr (Avenzoar, 1091-1162 AD) also dissected animals and described anatomy and physiology of various organs [7]. In 1242 AD, Ibn al-Nafis (1210-1288 AD) provided accurate descriptions of the circulation of blood in mammals [5]. His anatomical observations disproved some Galenic doctrines which were taken for granted for several hundred years. His experiment proved that the heart has two ventricles rather than three as stated by Galen. He also clarified that the nourishment of the heart is actually from the blood passing to it in the vessels situated in its substance rather than the heart is nourished by the blood present in the right ventricle as thought by Galen [2]. After 600 years of the death of Ibn al-Nafis, his contribution in medical science was highlighted by Muhyi-d-din At-Tatawi (1896-1945 AD) through presentation of his thesis entitled "Der Lungenkreislauf nach El-Korachi. Dissert, z.eil. d. Doktorwrde, Freiburg im Brisgau 1924" [8].

Animals used for establishing surgical procedures

The ancient Unani physicians carried out experiments on animals to establish certain surgical procedures before applying them in human being. Ibn Zuhr introduced animal testing as an experimental model for establishing surgical procedures. He performed tracheotomy on a goat and proved the safety of this surgical procedure in humans. He has given stress on the importance of sound knowledge of anatomy for the learners of surgery. Moreover, he insisted on a well organized training programme for medical students before allowing them to perform surgery independently [7].

Animals used for drug testing

Tiryaq (Theriac) is a semisolid dosage form which has been introduced by Magneeus Felsoof. Indrumakhas I (Andromachus I) has modified *tiryaq* by adding flesh of snakes in it and gave the name '*Tiryaq-e-Farooq*' [9] which has been found very much effective for the treatment of bite by poisonous animals specially snake, and has also been recommended for the treatment of other diseases such as leprosy, epilepsy, vitiligo, arthritis, jaundice, colitis, ascitis etc. Jalinus also did experiments on individual ingredients of *tiryaq-e-farooq* and stated that this is not only useful in the treatment of all cases of poisoning; even it is also very much beneficial for the treatment of other ailments. He further stated this compound preparation is specially given to strengthen all vital organs. Jalinus has also evaluated the efficacy and safety of *tiryaq-e-farooq* in animals. He took rooster [10] and divided them into two as control and test group; in control group, he did not give any treatment while in test group, he administered *tiryaq*. After that, he brought both groups into contact with snakes and he observed that the control group of animals which had not received any treatment died immediately whereas the test group of animals survived. Furthermore, Jalinus pointed out that such type of pre-clinical study may be useful to make sure whether the *tiryaq* is in its natural form or it has been adulterated [11]. Somewhere, it has also been mentioned that the experimental animal i.e. cocks for testing the efficacy of *tiryaq*, were bitten by beasts [12]. Abu-Bakr Muhammad Ibn Zakariya Razi (Rhazes, 865-925 AD), an eminent physician and acclaimed an author of nearly 200 medical and non-medical treatises [13]. It has been recorded that toxicity of drugs in animals carried out by him. Razi has tested the safety profile of mercury in monkeys which is documented by Ibn al-Baitar (1197-1248 AD) in his compendium '*Al-Jame al-Mufradat al-Advia va al-Aghzia*' [2], a large compendium dealt with more than 2300 single drugs [14]. Ibn Zuhr has carried out a pre-clinical trial to demonstrate the anti-ulcer and healing properties of a plant drug in sheep [2]. In India, such type of research in Unani Medicine was initially perceived by Hakim Ajmal Khan (1868-1927 AD). He engaged Dr. Salimuzzama Siddiqui to carry out research studies on medicinal plants used in Unani Medicine [15]. Under the guidance of Ajmal Khan, Dr. Salimuzzama Siddiqui did a pioneering work on *Rauvolfia serpentina* and separated three major constituents viz. *ajmaline*, *ajmalicine* and *ajmalicinine* in 1931AD [16]. Of them *ajmaline* has been proved to have significant antiarrythmic activity in rat model [17]. The antihypertensive, antiarrhythmic and hypocholesterolaemic effects of *Khameera Abresham Hakim Arshad Wala* have been evaluated in rats and rabbits by Siddiqui HH in 1963 AD [18]. Another study has revealed the significant cardioprotective effect of *Khameera Abresham Hakim Arshad Wala* in isoproterenol-induced myocardial necrosis in rats in a dose of 800 mg /kg/ day [19]. The evaluation of chronic toxicity of *Kushta Sammul Far* has been carried out in Wistar albino rats by Ansari *et al*, 2013. [20]. At present, many research studies are being carried out on animals to evaluate the safety and efficacy of single and compound drugs used in Unani Medicine.

Conclusion

Many renowned ancient Unani physicians such as Aristotle, Erasistratus and Galen have performed vivisections on animals for the study of anatomy and physiology of various organs and have also evaluated the structural abnormalities of many diseases. Ibn al-Nafis has demonstrated complete description of blood circulation in mammals. Ibn Zuhr has introduced animal testing as an experimental model for establishing surgical procedures before applying them in patients. The efficacy of *tiryaq-e-farooq* was evaluated in roosters. The toxicological study of mercury has been carried out in monkeys. Keeping in view aforesaid experiments, it may be concluded that animals were widely used in biomedical research in Unani Medicine since ancient times. Though, the frequency of biomedical research on animals in Unani Medicine was comparatively less, the most plausible explanation may be that most of the drugs used in Unani Medicine have been introduced on the basis of direct observations on human beings. Of late, animals are being very often used in Unani Medicine to validate the efficacy and safety of single as well as compound drugs. The above deliberation bears the testimony to the fact that

Unani system has always evolved itself over a period of time to be an evidence based medicine.

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