

Inhalation Therapy and Unani Medicine

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Abstract

It is tempting to think of inhalation therapy as a modern approach to drug delivery, but this would negate some thousands of years of history and literally hundred of ingenious devices and hopeful medications. The first recorded use of inhalation therapy is from ancient Egyptian Ebrus Papyrus (1554 BC). In Unani Medicine the Greek physician Hippocrates (460-370BC) advocated the inhalation of vapors of herbs. Over a thousand year later Zakariya Razi, an Arab physician commonly known as Rhazes in western world advocated the inhalation of vapor of arsenic. More recently at the end of the 12th century, Maimonides, the physician of Sultan Saladin recommended the inhalation of vapor generated from herbs thrown in to the fire for the treatment of asthma. In Unani Medicine inhalation therapy is in use from a very long time and in future it can be used more effectively by adapting the recent advancement in basic sciences and inhalation therapy. The present study attempts to summarize the basic principles of inhalation therapy and its use in Unani Medicine.

Keywords: Inhalation therapy, Unani Medicine, Bakhoor, Inkebab

Introduction

In Unani Medicine, there are three components of the treatment as according to Ibn-e-Sena "Indeed the treatment is completed by one of the three methods first of which is Tadbeer and Taghzia, second is the use of advia and the third one is the use of Aml-e-Yad."(Ibnesena, 1930; Ibnesena, 1995) The purpose of Ilaj-bit-Tadbeer is to evacuate the morbid material from the body or to transfer from a part to another and inhalation is one of them but now in today's scenario inhalation has been developed as an another route of drug administration in addition to a Tadbeer to evacuate the morbid material (Ibnesena 1995) and now inhalation is a term used for a variety of treatment techniques, including drugs administered via inhalation. It aims at targeting lung tissue, airway secretion and microorganisms in upper, central and/or peripheral airways. However, drugs targeting systemic effects are used aiming at deposition in the alveoli where it can be rapidly absorbed and distributed (Neville, 1977).

It is tempting to think of inhalation therapy as a modern approach to drug delivery, but this would negate some thousands of years of history and literally hundreds of ingenious devices and hopeful medications (Sanders, 2007). Inhalation of drugs was an easy and low cost method; hence it got a

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wide use in medical therapy during that time (Shehata, 2009). Credit goes to ancient Egyptians for the first preparation of therapeutic materials for inhalation therapy. The inhaled material was in the form of smoke, vapour or volatile oils, obtained from the powdered dry plants or minerals, for the relief of nasal, throat and chest troubles (Shehata, 2009; Doghaim, 1972). Ancient people recognized the good therapeutic effect of many substances that were used for inhalation therapy in the form of snuffs, vapours or smoke. These substances were preserved in pottery pots and placed on pottery jars when used for inhalation (Doghaim, 1972).

Inhalation Therapy in Ancient Medicines

In ancient time local therapy was the prevailing means of treatment in ancient time, so nearly all respiratory troubles were treated by one form or other of inhalation. Inhalation of powder, smoke or vapour of the dry, burnt or boiled medications was well known at that time (Shehata, 2009). Ancient Egyptians were the first to use of inhalation therapy for the treatment of the oral, pharyngeal and chest troubles. Many prescriptions in the Ebers and Berlin medical papyri, written four thousands years ago report the first use of inhaled dried medicinal plants boiled medications or the smoke of some burnt, material, in the form of nasal snuff, oral insufflations or vapour inhalation (Shehata, 2009; 2012).

The Babylonian civilization was contemporary to the old Egyptian era. Physicians were known to many drug prescriptions and use them by different means of inhalations (Shehata, 2012). In ancient India, physicians used some forms of drug inhalation. The well known one was *Cannabis indica*. The Indians were the pioneer users of burnt Indian hemp (*Cannabis, indica*) for medicinal purposes (Shehata, 2012; Baraka 1982).

Inhalation Therapy and Unani Medicine

In Greek medicine, the use of burnt incense was very extensive, besides the inhalation of many dried plants. In ancient Greece, the physician Hippocrates advocated the inhalation of vapours of herbs and resins boiled with vinegar and oil which were then drawn into the lungs through a tube (Shehata, 2009; Sanders, 2012). The great Greek physician Galen (130-201 A.D.) described some powdered drugs their volatile vapour and smoke through inhalation for the relief of nasal and head troubles (Shehata, 2009).

The Romans established general public baths, in their large cities in which warm water was available. The evolved warm steam in such places was in use

for many medicinal purposes and was very helpful for the relief of many body troubles (Shehata, 2009; Reginald, 1982).

The Arab civilization that began at the eighth century added a lot of progress to inhalation therapy. They introduced new medicinal plants in this form of therapy as the Eucalyptus, Peppermint, Cinnamon, Fenugreek, Black reed and the prepared liquid of Benzoin, Thymol and Violet. The medicinal plants were in use in the form of powder for sniffing, volatile vapour for inhalation or burnt smoke for breathing. The dried leaves, roots or barks of these plants were the material for inhalation for the treatment of nasal, throat, larynx, and respiratory troubles besides the relief of several head and body troubles (Ibnesena, 1930, 1995; Reginald, 1982).

The eminent Arab physician Rhazes (850-932 AD.) used the powdered narcotic plants, Opium, Hyocyamus, Mandrake and Henbane, imbibed in a sponge to be inhaled for general anaesthesia before any surgical operation. He also advocated the inhalation of vapour of arsenic for many medicinal purposes (Sanders, 2007; Razi, 1998).

The Arab Physicians revolutionized the inhalation therapy in technique and indications. They were first to develop the inhalation anesthesia in the 9th century under the name of Al-Marquad. In this method the drugs were dissolved in water and imbibed by sponge, to be used by inhalation at surgery. This inhalation anaesthetic method was first described by the Arab physician Isa Bin Ali (Shehata, 2009; 2012).

The first early trial for resuscitation of camatosed patients by drug inhalation through forced respiration by a manual bellow was practiced by the Arab physician Saleh Bin Behla. That was reported for the first time at the ninth century (Shehata, 2009; Shehata, 2012).

Arabs also modified the use of Hammam by adding volatile medicinal plants to the warm water and the patients were submerged to the level of the neck in warm water, covered by a blanket to retain the vapour for inhalation (Reginald, 1982).

The Persian physicians were also well known to inhalation therapy. Their well known king and physician Jamshid described the inhalation of the volatile vapours of boiled roses, musk, eucalyptus and ambergris for the relief of respiratory troubles (Anonymous, 2012).

In 1190 AD, a famous Spanish physician and philosopher Maimonides (Physician to the Sultan Salahuddin Ayuobi) wrote *Treatise on Asthma* and

recommended inhalation of fumes generated from herbs thrown on a fire (Sanders, 2007; Maimonides, 1963).

There are many methods employed in Unani Medicine for the inhalation therapy. Their short description is as follows:

1. Bakhoor Dhooni (Fumigation): Some drugs are burnt and their smoke is introduced to a particular place. This is also called Tadkheen
2. Inkabab, Baphara (Vopourbath): Some drugs or simply water is boiled and their vapour is introduced to a particular site.
3. Shamoom (Olfaction or smell): The drug, which is smelled and its volatile constituents reaches through the nose.
4. Lakhlakha (Inhalation): These are either watery or solid drugs, which are kept in a wide mouth container or bottle and smell reaches not only to nose but air passages also (Kabir, 2002).

The tools for inhalation therapy are large clay pots for volatile oils, metal containers for boiling liquids and wood snuff box for powdered drugs. For vapor inhalation the liquids are boiled or hot stones are used for producing the Bakhoor and the evolved vapor received by the patients under a blanket (Ibnesena, 1995; Ibnesena, 1930).

Advantage of Inhalation Therapy

Conventional therapy for respiratory diseases consists of administering therapeutic agents by the oral or parenteral route. However, the amount of drug reaching the site of pathology may be small due to poor pulmonary distribution of most systemically administered drugs. Delivering drugs by inhalation directly to the lungs results in local drug concentration far higher than that achievable by either oral or parenteral administration. Relatively small doses are required for effective therapy, reducing systemic exposure to drug and thus minimizing adverse effects. Lower dosage regimens may provide considerable cost savings, especially with expensive therapeutic agents. Delivering small doses of active ingredients directly to the lung effectively targets the drug, thereby maximizing therapeutic effect while minimizing adverse effects. A drug having narrow therapeutic window or requiring prolonged treatment regimen by conventional routes of administration, when administered by the inhalation route would have reduced systemic exposure and toxicity. Consequently, this approach may be advantageous where the patient's system is overburdened with the traditional range of chemotherapeutic agents (Anonymous, 2011; Moritz, 2011; Khilnani, 2008; Raiser, 1986).

On the other hand, the large surface area for absorption and the relatively low metabolic activity of the lungs make this organ system a potential route for the systemic delivery of drugs that cannot be delivered by other means. Many studies have shown that the lungs provide substantially greater bioavailability for macromolecules than any other port of entry to the systemic circulation.

Thus the advantages of inhalation therapy are:

- The inhaled route is the most effective method to get the medicine where it is supposed to go– directly to the airways
- The therapeutic relief is rapidly achieved – especially symptom relief with inhaled bronchodilators
- The intake is low and a fraction of the oral dose is enough for the desired result.
- Side effects are minimal since rest of the body is not exposed to the drugs.
- Some drug when taken through oral route become inactive while passing through digestive process.
- Since chronic respiratory diseases require long term treatment, the exceptional safety of inhaled therapy is especially valuable (Anonymus, 2011; Moritz, 2011, Khilnani, 2008; Raiser *et al.*, 1986; McDonald, 2005).

The Lung as a Route of Application for Systemic and Local Therapy

Although the lung represents effective barrier systems and clearance mechanisms, much attention has been raised in the last decades to this organ for drug delivery applications.

The first reason is its large absorption area. The lung build up a total surface of ~100m² that is enveloped by an equally large capillary network, from which many agents can be readily absorbed to the bloodstream avoiding a first-pass effect of the liver (Raiser *et al.*, 1986; Patil *et al.*, 2012; Agu *et al.*, 2001).

Another reason is the known instability and low permeability of proteins and peptides when these biopharmaceuticals are administered through the widely preferred oral route. Consequently, most proteins and peptides on the market are administered intravenously. But the parenteral route of application does generally not meet with patients' convenience and compliance, in particular because the indication for the use of these agents is usually treatment of a chronic disease requiring frequent injections. Thus, the pulmonary route of application offers a noninvasive alternative for systemic therapy (Raiser *et al.*, 1986; Patil *et al.*, 2012; Agu *et al.*, 2001).

Drug Properties affecting Inhalation Therapy

Drugs for inhalation therapy are administered in aerosol form. An aerosol is defined as a suspension of liquid or solid in the form of fine particles dispersed in a gas. The ability of the aerosolized drug to reach the peripheral airways is a prerequisite for efficacy. The factors which influence the particles deposition in the respiratory tract include impaction (inertial deposition), sedimentation (gravitational deposition), brownian diffusion, interception, and electrostatic precipitation (Khilnani, 2008; Raiser *et al.*, 1986; Hiller *et al.*, 1981; Edward *et al.*, 1998; Behera, 2005).

Therapeutic effect of inhaled drug can be attributed to a variety of factors;

- Inhaled aerosol particles must possess a very narrow range of “aerodynamic diameters” to pass through the filter of the mouth and throat.
- Even if properly designed and produced, aerosol particles may be propelled with too high a velocity and consequently deposited in the mouth and throat by inertia.
- Once in the lungs, particles must release the therapeutic substance at a desired rate and,
- Escape the lungs’ natural clearance mechanisms until their therapeutic payload has been delivered.

Effect of Particle Size : For locally-acting drugs, the particles need to be deposited in the area of the respiratory tract requiring treatment. For systemically- acting drugs, particles need to reach the alveoli for absorption. Large particles (5-10 μm) do not follow changes in the direction of airflow and are deposited by inertial impact in the upper airways. Particles deposited in the mouth and throat can be swallowed and lead to local or systemic side effects. Intermediate-sized particles (3-5 μm) can be carried further, into smaller airways of the bronchi and bronchioles. Small particles (<3 μm) behave more like gas molecules and follow the airflow all the way to the alveoli. The very smallest particles (<0.5 μm) can fail to be deposited in the alveoli, and portions of the medicine can resultantly be exhaled. Controlling the air velocity by slow inhalation will maximize the number of particles that reach the alveoli (Khilnani, 2008; Raiser *et al.*, 1986; Hiller *et al.*, 1981; Edward *et al.*, 1998; Behera, 2005).

Fate of Drug Given Through Inhalation Therapy

The efficacy of drugs used through inhalation method depends on their local effects in the airways. Thus, achieving a high local concentration of these

agents in the lung should maximize their intended effects and minimize their systemic absorption and potential adverse actions. About 15-40% of drug released from an inhaler device is deposited in the lungs. This is more than sufficient to achieve a clinical effect. The portion of the drug that is deposited in the lungs has its pharmacological effect and is then absorbed from the lungs into the systemic circulation (Anonymous, 2011).

Drug deposited in the throat is swallowed and subsequently absorbed from the gastrointestinal tract into the systemic circulation via the liver where it undergoes metabolism and subsequent elimination (Anonymous, 2011).

Modern Drug Delivery System for the Inhalation Therapy

Inhaled drug delivery systems can be categorized into three main groups on the basis of how the aerosols are generated and each group with a unique strength and weakness. For the purpose of inhalation therapy an aerosol of the drug can be generated in three ways:

- Pressurised Aerosol System
- Dry powder system
- Nebulisers (Reiser *et al.*, 1986; McDonald *et al.*, 2005 ; Behera, 2005 ; Tripathi, 2003)

Pressurized Aerosol System

They are also called metered dose inhaler because it delivered a specific quantity of drug to the lung. The MDI is a device that delivers a specific and pre-metered amount of medication to the lungs, in the form of an aerosol spray that is inhaled by the patient. It consists of a canister of pressurized medication that fits into a plastic actuator sleeve and connects to a mouthpiece. The formulation in an MDI is made up of the drug and a liquefied gas propellant.

Proper use of the MDI requires some practice. Unless the MDI is used correctly, the patient will not get the full dose of the drug and, hence, will not derive the full benefits. Many patients, including children, find it difficult to coordinate the actuation and inhalation of the drug released from the MDI. Such patients can benefit immensely by using a spacer attached to the mouthpiece. MDI + spacer are generally as effective as a nebulizer (Reiser *et al.*, 1986; McDonald *et al.*, 2005; Behera, 2005; Tripathi, 2003).

Dry Powder System

Dry powder inhalers (DPIs) are devices through which a dry powder formulation of an active drug is delivered for local or systemic effect via the

pulmonary route. The drug in a DPI is provided as micronized powder (particle size 2.5-5 μm) with an inert carrier such as lactose. DPIs are breath-activated devices and, unlike the MDIs, do not require coordination between actuation and inhalation. The patient exhales out a full breath, places his/her lips around the mouthpiece, and then quickly breathes in the powder. DPIs are easy to use and as effective as MDIs (Reiser *et al.*, 1986; McDonald *et al.*, 2005; Behera, 2005; Tripathi, 2003; Alagusundaram, 2010; Peart *et al.*, 2001).

Nebulisers

The nebulizer converts the drug solution into a continuous fine aerosol mist, which can be inhaled directly into the lungs via a face mask or mouthpiece. Nebulizing chambers are small plastic devices into which the drug solution is placed. These devices are driven by a compressor (electric/battery operated) or oxygen. A gas flow of about 6-8 liters/minute is normally required to drive the nebulizer. In this Drug inhalation is accomplished by normal tidal breathing over a 5-10 minute period (Reiser *et al.*, 1986; McDonald *et al.*, 2005; Behera 2005; Tripathi 2003).

Future of Inhalation Therapy in Unani Medicine

The value of inhalation as a route of drug administration has been recognized for thousands of years in Unani Medicine and it is in use as route of drug administration from the time of Hippocrates. One of the earliest inhaler devices is a design attributed to Hippocrates (Greece, 460–377 BC) that consisted of a simple pot with a reed in the lid, through which vapors could be inhaled.

Commonly used materials for the inhaled remedies include plants with anticholinergic properties, such as datura, henbane, lobelia, and belladonna, in addition to arsenicals, balsams, and gum resins. As in the Unani system of medicine, there are many drugs, which are used in the management of asthma; they can be used more effectively by adapting inhalation as a main route of drug administration especially for respiratory diseases.

On identifying the particular constituent responsible for the bronchodilator and anti-inflammatory properties and in which particular solvent that constituent or most of the constituent of that particular plant is dissolved, drug can be obtained in the liquid form or get dried in the form of fine powder depending on the type of device is to be used. The volatile oil component of the drug may be use through inhalation therapy with a suitable vehicle.

Drugs used in Unani Medicine through Inhalation Therapy			
Name of Drug	Botanical Name	Parts Used	Method Used
Ward	Rosa damascena Mill	Oil	Inhalation
Dhatura	Datura innoxia Mill.	Leaves	Tadkheen
Zaitun	Olea europea Linn.	Olive with nuts	Fumigation
Kibrit	Sulfurem		Fumigation
Tanbul	Piper betle Linn	Leaves	Fumigation
Ma'a	Water	Water vapour	Inkabab
Yasmin	Jasminum grandiflorum Linn	Oil, flower	Inhalation
Qaisus	Cistus creticus Linn	Extract	Sniffing
Qinnah	Ferulah galbaniflua Boiss et Bushe	Gum	Bakhoor
Cumin	Cuminum cyminum Linn	Seed	Inhalation

Conclusion

Information regarding the therapeutic use of inhalation therapy can be traced back to the period of Hippocrates and other Unani physician of early ages. Although the modern scientific technique and knowledge of exact pathological changes were not known at that time but on the basis of the clinical understanding of different diseases, there were various forms of inhalation therapy that may be correspond to the latest techniques of currently available inhalation therapy.

Use of a number of drugs in various inhalation techniques like *Bakhoor (Dhooni)*, *Inkabab (Bhapara)*, *Shamoom Lakhlakha* etc were in vogue during Arabic and pre- Arabic era of Unani Medicine. The rationale behind the application of such therapies was of course the early onset of action, selectivity and specificity of the drug. Such therapies if brought into the practice using the latest technical know how about the physico- chemical properties of the drug constituents and its effective application so as to reach the desired site may proved to be revolutionary in the management of respiratory medicine and beyond.

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