

**NANO-MATERIALS: A SCIENTIFIC APPROACH TO VALIDATE AN ANCIENT
DOSAGE FORM THE “CALX (KUSHTA) IN UNANI MEDICINE”**

Talha Mushtaq* and Abdul Hannan

Research & Development Department Hamdard Laboratories, Karachi, Pakistan.

***Corresponding Author: Talha Mushtaq**

Research & Development Department Hamdard Laboratories, Karachi, Pakistan.

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ABSTRACT

Nanotechnology is an innovative scientific technique in the 21st century. By analyzing the connection between nanotechnology and natural medicine, the utilization of Nano innovative strategies can be improving bioavailability of Unani medications. It is demonstrated that nanotechnology is one of the fastest, the most potential and the extensively high and new innovative procedure in the present period, and it greatly promotes the improvement and bioavailability of Unani/herbal drugs. It is noted that 80% of the total population has faith in herbal medications, mainly plant-based medications for their necessary healthcare. Unani medications generally introduce in the market in conventional dosage structure but, now different rational methodologies of Nanotechnology are being built up now a day to deliver natural medicine because of their poor rate of absorption and target explicit approach. In Unani Medicine. Kushta (Calx), the most ancient form of Nano-medicine is utilized since 1000 BC. The majority of the Plant actives are ineffectively absorbable in view of their hydrophobic behavior. This nature of constituents leads to reduced bioavailability and required repeated administration or increased dose, and thus limits the clinical use of Unani medications. Unani Medicine has the technique to change over them either into carbonates or oxides. The oxide structure is actually known as Kushta (Calx) and the procedure of transformation is known as Taklees (calcination). The breakthrough in this respect will be accomplished from the exploration of the nanomization of Unani medications against malignancies and various other disorders.

KEYWORDS: Nanomaterials, Conventional Medicine, Kushta (Calx).**1. INTRODUCTION**

Unani system of medicine, broadly known in the middle east as tibb, is a widespread health care system that incorporates theoretical understanding and applied. It rests on the universal laws as understood by ancient Egyptians and Greeks, as well as Arabs and non-Arabs of the middle ages. They produced a coherent and inter related medical system where science and philosophy were engaged simultaneously to create a comprehensive understanding of health and disease. Tibb is recognized by World Health Organization as one of the alternative system of medicine (see www.who.int/medicines/en: accessed December 10, 2012). The systems roots can be traced back to ancient Egyptian, however, the earliest surviving complete works are those of the great Unani physicians Hippocrates (ca. 460 BCE – 370 BCE) and Galen (ca. 129 CE), who both studied drugs in Egypt. Arabs and Muslims physicians such as Rhazes and Avicenna further developed Unani medicine from their own experience and pertinent observation. Avicenna also integrated Chinese and Indian (ayurvedic) medical knowledge. Like other traditional system of medicine, Unani Medicine follows holistic approach to health

maintenance, diagnosis and restoration of health. In Unani Medicine, Kushta (Calx), the most prehistoric form of Nano-medicine is utilized since 1000 BC. Unani Medicine has the technique to change over them either into carbonates or oxides. The oxide structure is actually known as Kushta (Calx) and the procedure of transformation is known as Taklees (calcination).

From ancient age to the modern era, the medicinal properties of metals play vital role in Unani Medicine, but can be toxic if it is use in excess. Most of the metals are naturally occur as minerals. However, heavy metals are essential to some simple and polyherbal formulations of Unani medicine and are been used for eras. Unani formulations having metals are formed after many purification methods of metals like soaking, filtration, washing, powdering, heating, trituration, coating, detoxification etc. After this, the metals in the finished products do not possess toxicity. ‘Kushta’ is derived from word ‘KUSHTAN’ (a Persian word) means ‘killed or conquered’. Kushta (Calx) is one of the most imperative dosage forms in the Unani system of medicine. Kushta is the Nano fine particles of the Unani

preparations acquired by the process of Taklees (calcination) of elements, mineral and animal drugs. These preparations, by different process are calcined in closed pots and in rock bottom of different sizes, with different intensity of heat. According to the ancient Unani scholars these calcination techniques used in calx preparation are particular processes in which herbal juices are added during preparation. These procedures increase the effectiveness of preparation and also remove the toxicity of the elements. Thus, Kushta is stated to a Nano material or substance that has been prepared by killing / burning of metals / minerals at high temperature upto (700 - 800 °C).

Calx is a dosage form, which is effective in a very lesser dose and with rapid action because of its fast absorbing ability. Though, this dosage structure has long been used and is claimed to be very effective, but serious attempts have not been made to study and standardized it on scientific basis because of lack of attention of scientific community towards its standardization. In spite of the fact that kushta is used for eras without any evident side effects and is well-known in Unani system of Medicine, very few scientific studies have been carried out. Six metals were used by ancient Physicians gold, silver, copper, tin, lead, and iron. Majority of these metals are used in Unani formulations (see Table 1) It is noted that 80% of the total population has faith in herbal medications, principally plant-based medications for their necessary healthcare. Unani medications generally introduce in the market in conventional dosage structure but, now different rational methodologies of nanotechnology (see Table 2) are being built up now a day to deliver natural medicine because of their poor rate of absorption and target explicit approach.

1.1 Objective

The objective of this paper is to validate an ancient dosage form practice in Unani system of medicine by the old concepts of kushtajat in modern understanding, To Identify modern technologies that can be applied to testing the calx, Exploration of the nanomization of Unani medications against malignancies and various other disorders, providing possible explanation and recommendations to initiate research in this area of potential therapeutic value.

1.2 Historical Time Line

1 Period of Hermis (Alchemy)

A guiding principle of alchemy was the *transmutation of elements*. Use of metals and minerals dates back (2000 years) to the time immemorial. It should be known that for long ago, this dosage form was in practice in Greece and Italy.

2 Galen (2nd C A.D.)

Galen states, that the efficacy of burnt lead is un parallel in Cancer and copper was burnt before its use because it is harmful for the body when use as it is.

3 Aribasus (326-403 A.D)

Used ash of animal

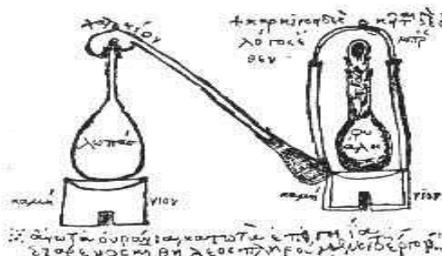
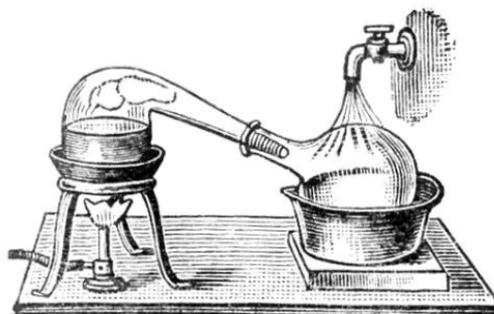
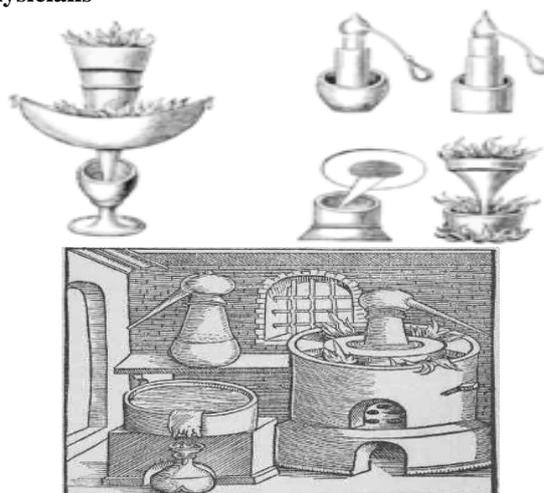
4 Jabir ibn Hayyan (721- 813 AD)

Geber in his book nakhbe jabri has mentioned the use and method of preparing of kushta of iron, tin, ammonium chloride and mica, Sublimation of mercury and Sulphur.

5 Al-Razi (925 A.D.)

1. In his book Sirr al-Asrar, Razi divides the subject of "Matter" into three categories, as in his previous book al-Asrar. Knowledge and identification of the medical components.
2. Knowledge of equipment and tools of interest to and used.
3. Knowledge of seven chemical procedures and techniques like sublimation and condensation of mercury precipitation of Sulphur, and arsenic calcination of minerals (gold, silver, copper, lead, and iron), salts, glass, talc, shells and waxing

1.3 Various Experimental Instruments Used by Unani Physicians



2. Nano drug delivery system (NDDs) necessary for Unani Medicine

NDDs be present a selection to overcome the drawbacks of the traditional Unani Medicine drug delivery systems because of the following reasons:

- Nanoparticle can be used to target the Unani Medicine drug to individual organ which increases the selectivity, drug delivery, efficacy and safety.
- Nanoparticles can be applied to increase the natural drug solubility.
- Better efficacy.
- Able to deliver high concentrations of medicines to disease locations because of their exceptional size and high loading capabilities.
- Transporting the drug in minor particle size improves the whole surface area of the drugs thus allocating faster dissolution in the blood.
- Decreases the side effects.

Nano systems can deliver the active constituent at a sufficient concentration during the entire treatment period, directing it to the desired site of action. Conventional treatments do not meet these requirements.

Several Nano technological strategies, such as polymeric nanoparticles, solid lipid nanoparticles (SLNs), liquid crystal (LC) systems, precursors systems for liquid crystals (PSLCs), liposomes, and micro emulsions, have tried to break this barrier, they allow materials with diverse properties to be used in the same medicinal preparation, and may even alter a substance's properties and behavior in a organic environment. These technological innovations have modernized drug delivery. The NDDs have the capability not only to increase the efficacy of active constituents, but also to restore other constituents that were cast-off because they were not useful in preparation. Furthermore, the capacity to improve new substances, such as by increasing efficacy, decreasing side effects, and adjusting the release of active constituents, before they are presented to the market or used therapeutically, makes this methodology even more attractive. Pharmaceutical Drug industries have become progressively involved in Nano technological advances because these developments provide advantages, such as the potential to develop new formulations.

3. Sources of Nano Constituents From Unani Floras:

Nanoparticles of numerous proportions and shape have been manufactured from different parts of plant like stem, root, leaves, fruit, seed etc.

4. Synthesis of Nanoparticles

4.1. The Traditional Classical Method

Unani scholars have clarified various procedures of Kushta preparation. They revealed several detoxification routes, distinguished between perfect and imperfect Kushta, recorded ways to turn Naqis Kushta (incomplete

calx) to Kamil Kushta (complete calx). All these ways and means were the classical means of 'Process and Product Standardization'. Additionally, the clear hints on the usage of Kushta have been instructed. (See table 1). Before using the metallic compounds, they are always subjected to procedures called 'tasfiya' (purification). This is an idea to get rid of the impurities and their harmful qualities. If 'tasfiya' is not done, their use is said to be damaging and injurious to the individual.

The Unani physicians believe that the repeated purification methods employed during preparation reduces the toxicity. Further medicine is finely grounded in pestle and mortar with specified juice. Then mixture is wrapped in a clay pot and calcinated in closed vessel in pits of diverse sizes, provides different intensity of heat. The process is repetitive till kushta is obtained. Metals and minerals are commonly not used directly in the raw form but are transformed either into their carbonates or oxides by the process of Ibraq or Taklees (calcination), the product obtained is known as Kushta (calx). Standard stepwise techniques of manufacturing kushta given below, if it is followed accurately, it gives a consumable dosage form for human beings.

1. Collection of raw herbs
2. Soaking: In Soaking method, Transformation effects take place, alkaloid binds with metals and other compound used in kushta, physicochemical changes take place in the presence of water and air.
3. Trituration: It helps in particle size reduction and conversion, enables heat transformation (conduction & convection), increases binding properties, aids uniform mixing.
4. Drying
5. Gile Hikmat: This process involves in sealing the vessel or pot by wet china clay, prevents interference of outside gas and dirt
6. Heating: Causes binding of herbal and mineral ingredients, development of Nano particles, firm, substantial, solid converts into brittle, light soft substance. Therapeutic value also increases and carbonate, oxides and sulphides are formed.

4.2 The Modern Method

The most recent research in nanotechnology is intensive on nanomization of natural plant extracts and take diversified benefits. Many techniques are used to make nanoparticles by using herbal extracts i-e High-pressure homogenization method, Complex coacervation method, Co-precipitation method, Salting-out method, Solvent displacement method and Super critical fluid method. The High-pressure homogenization method techniques commonly used for the formulations. In this technique, the lipid is pressed with high pressure (100 to 2000 bar) through a very high shear stress, which results in distraction of particles down to the sub micrometer or nanometer range. High-pressure homogenization method is a very consistent and powerful technique for the significant production of nanostructured lipid carriers, lipid drug conjugate, SLNs, and parenteral emulsions

Table 1: List of some Kushtas (Calx) used in Traditional Unani Medicine.

Elements	Unani Preparation	Ingredients		Uses
		Mineral	Herbal	
<i>Tin</i>	Kushta Qalai	Tin	Aloe barbadensis	Impotence
<i>Iron</i>	Kushta Kubsul-Hadid	Iron oxide	Aloe barbadensis Embelica officinalis Teminelia belerica Terminalis chebula	Anemia and general debility
<i>Zinc</i>	Kushta Jast	Zinc oxide	Aloe barbadensis	Spermatorrhoea, leucorrhoea, and impotence
<i>Calcium</i>	Kushta Busud	Coral roots	Aloe barbadensis	Bleeding disorder and leucorrhoea
	Kushta Sadaf	Oyster shell	Rosa damascene	Cardio tonic
	Kushta Marvareed	Pearls	Rosa damascena	Cardio tonic
<i>Tin</i>	Kushta Qalai	Tin	Aloe barbadensis	Impotence
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<i>Calcium</i>	Kushta Busud	Coral roots	Aloe barbadensis	Bleeding disorder and leucorrhoea
	Kushta Sadaf	Oyster shell	Rosa damascene	Cardio tonic
	Kushta Marvareed	Pearls	Rosa damascena	Cardio tonic

5. Classical General Tests for Standardization of Calx

- Floating Test: Floating of (Calx) kushta on surface of water if small quantity of kushta is sprinkled
- Fineness Test: It should be so much fine that on rubbing a small quantity of the sample between the fingers it should enter into the lines and creases on the fingers.
- Fuming Test: It should not produce fumes when put on fire.
- Tastelessness: No taste should be observed of kushta.

6. Modern Techniques for Standardization of Calx

In this Modern Era, Use of Technology is becoming more easy and popular. The various modern analytical methods for Standardization of Calx are as follows

- Microbiological Evaluation
- Heavy Metal Estimation
- Atomic Absorption Spectro-Photometry (AAS)
- X-ray Diffraction (XRD)
- X-ray Crystallography

7. Types of Nanoparticles

Nanoparticles can be classified into different types according to the size, morphology, physical and chemical properties. Following NPs are described in Table 2.

- Biodegradable Polymeric nanoparticles
- Solid lipid nanoparticles
- Metal and inorganic nanoparticles
- Nano-liposomes
- Nano gels

8. Strategies of Nanotechnology as Novel Drug Delivery system

Drug delivery system made a NDDS, a novel method to overcome the disadvantages of the traditional drug delivery systems.

Nano-sized delivery system was selected because of the following reasons:

- Able to transport high concentrations of drugs to disease sites because of their unique size and high loading capabilities.

- Deliver the medicine in the minor particle size that improves the entire surface area of the drugs giving quicker dissolution in the blood.
- Reduction in the side effects.
- Decrease in the amount of the drug preparation

Table 2: List of Different types of Nanoparticles (NPs).

S.No	Type of Nano Particles (NPs)	NPs Size	Application	References
1	Biodegradable Polymeric nanoparticles	10–100 nm	Specifically applied for Nano spheres and Nano capsules In cancer, targeted polymeric NPs can be used to deliver chemotherapies to tumor cells with greater efficacy and reduced cytotoxicity on peripheral healthy tissues.	(Mallakpour, 2016 Vol.10, No.11 (2016) 895–913) (Juliana M Chan, 2010)
2	Solid lipid nanoparticles	10 and 1000 nm	SLNs are made up of solid lipid, emulsifier and water/solvent. The lipids used may be triglycerides (tri-stearin), partial glycerides, fatty acids (stearic acid, palmitic acid), steroids (cholesterol) and waxes (cetyl palmitate). Broadly investigated for topical application of actives for various skin diseases.	(S. Mukherjee, 2009)
3	Nano-liposomes	20 nm to several micrometers	Nano liposome refer to a lipid vesicles, applied for many purposes in the pharmaceutical, cosmetic, and food industries. Attributes of liposomes include their biocompatibility, biodegradability, non-immunogenicity, non-toxicity, and ability to entrap both hydrophilic and hydrophobic compounds. Targeted therapy can also be achieved efficiently via liposomes and Nano liposomes employing passive or active targeting mechanisms	(Khosravi-Darani, March 2010) (Corrêa, 2019)
4	Metallic Nanoparticles	1-100 nm	Metal nanoparticle is used to describe nanosized metals with dimension. There are various liquid phase methods for preparing metallic nanoparticles, such as chemical reduction and sol gel. These are used in therapeutic drug, gene and radionuclide delivery, radio frequency methods for the catabolism of tumors via hyperthermia, and contrast enhancement agents for MRI.	(Chakraborty, 2016)
5	Nanogels	Sub-micron size	Nanogels are three-dimensional formed by physical or chemical polymers. Nanogels have been discovered as drug delivery systems due to their valuable properties, such as biocompatibility, high stability, particle size, drug loading capability, that identify receptors on the target cells or tissues.	(Hamblin, 2019)

9. CONCLUSION

Nanotechnology has the ability of self-targeting without the connection of a specific ligand, the nanoparticles can be used for aiming targeting approach, due to their uniquely small size, at the pathological areas. Management of chronic diseases like cancer using targeted drug delivery nanoparticles is the modern accomplishment of nanotechnology. By evaluating the association between nanotechnology and natural medicine, the application of nanotechnological systems for bioavailability improvement of Unani/herbal drugs. In Unani Medicine. NDDs of herbal drugs have a prospective future for improving the activity and overcoming difficulties associated with Biological and natural medicines.

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