

## Medical and Scientific Bases of Wet Cupping Therapy (Al-hijamah): in Light of Modern Medicine and Prophetic Medicine

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### Abstract

Wet cupping therapy (WCT) is a simple and economic treatment that still needs scientific interpretation. It treated effectively diseases with different etiologies and pathogenesises e.g. rheumatoid arthritis (RA), hypertension, migraine, carpal tunnel syndrome (CTS), fibromyalgia, cellulitis and others. Here, we review medical and scientific bases underlying cupping therapy and introduce Taibah theory as a novel evidence-based scientific mechanism to explain it. Briefly, in Taibah theory, WCT is a minor surgical excretory procedure related scientifically to the principles of renal glomerular filtration and abscess evacuation, where a pressure-dependent excretion of causative pathological substances (CPS) occurs. CPS include disease-causing substances and disease-related substances (that result during disease pathogenesis). Negative pressure applied to skin surface causes local collection of filtered and interstitial fluids containing CPS at skin upliftings inside cups. Scarifying skin upliftings followed by cupping causes a pressure gradient and a traction force across the skin and capillaries to excrete collected fluids with CPS and cause bleeding at puncture sites. This increases filtration at both capillary ends and causes clearance of blood and interstitial spaces from CPS. WCT benefits from the suction pressure, phenomenon of reactive hyperemia, nitric oxide production and skin scarifications (openings in skin barrier) in enhancing natural excretory skin functions, improving lymphatic and capillary circulations and restoring homeostasis. Reported CPS of RA include autoantibodies, immune complexes, soluble interleukin-2 receptors, inflammatory mediators, certain cytokines, prostaglandins, toxic cellular products and rheumatoid factor, while CPS of CTS include malondialdehyde, interleukin 6, prostaglandin PGE- 2 and progressive edema (causing pain). WCT-induced filtration pressure may excrete those CPS in cupped blood.

Prophetic medicine (related to Prophet Mohammad peace be upon him) recommends WCT: "The best among what you use in therapy is Al-hijamah (prophetic method of WCT)". In conclusion, WCT has scientific bases in treating different diseases being the only treatment that clears blood and interstitial fluid from CPS. Therapeutic benefits of WCT is related to the amount of excreted CPS not the amount of letted blood.

**Keywords:** Cupping therapy; Prophetic medicine; Taibah theory; CPS; Rheumatoid arthritis; Hypertension

**List of abbreviations:** ATP: Adenosine Triphosphate; CGRP: Calcitonin Gene-Related Peptide; CPS: Causative Pathological Substances; CTS: Carpal Tunnel Syndrome; DMARD: Disease Modifying Antirheumatoid Drugs; NK Cells: Natural Killer Cells; NO: Nitric Oxide; NOS: Nitric Oxide Synthase; RA: Rheumatoid Arthritis; RBCs: Red Blood Cells; RF: Rheumatoid Factor; ROS: Reactive Oxygen Species; SII-2R: Soluble Interleukin-2 Receptors; TCM: Traditional Chinese Medicine; TNF: Tumor Necrosis Factor; VEGF: Vascular Endothelial Growth Factor; VIP: Vasoactive Intestinal Polypeptide; WBCs: White Blood Cells; WCT: Wet Cupping Therapy

### Introduction

The main target of scientific research related to medicine, drug discovery and disease treatment is to identify better therapeutic lines for human diseases and to improve quality of life without ignoring the economic aspect of treatment. Pharmacological treatments to human diseases act through introducing drugs to human body via different routes of administration. There are few lines of conventional medical treatment to act through withdrawing harmful inflammatory mediators, biological, chemical or other unwanted substances from human body. Unfortunately, modern medicine, medical practice and research concentrate more on treatments that are introducing new drugs and chemicals to human body without giving similar effort to treatment lines that may withdraw harmful substances. In light of the persistent incurable medical problems to date and the progressively increasing number of patients worldwide, we found it convenient

to shed light on one of the most controversial lines of treatment among medical practitioners that is cupping therapy. In this article, we will review cupping therapy, while paying special attention to the most important point regarding cupping therapy that is its scientific mechanism of action. Many of the misconcepts raised about cupping therapy arise from lack of understanding of how it works and to what extent it may be beneficial. Searching for a better conservative economic and effective line of treatment for pain conditions and other unrelated diseases forced us to search the literature extensively to investigate how beneficial cupping therapy is and to what extent. It is worth noting that Loukas et al. attracted attention of researchers to the scientific values that can be gained from studying religious texts. Loukas et al. reported that prophetic medicine (related to Prophet Mohammad peace be upon him) recommended cupping therapy as a treatment: "If there is a benefit in any of your treatment modalities, benefit will be in the blade puncture in cupping therapy, a gulp of honey and cauterizing, but I do not like cauterization" [1]. This motivated us to search and establish

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Received May 14 2013; Accepted May 28, 2013; Published May 31, 2013

**Citation:** El Sayed SM, Mahmoud HS, Nabo MMH (2013) Medical and Scientific Bases of Wet Cupping Therapy (Al-hijamah): in Light of Modern Medicine and Prophetic Medicine. Altern Integ Med 2: 122. doi:10.4172/2327-5162.1000122

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a novel simple evidence-based scientific mechanism to find answers regarding how cupping therapy works and how effective is cupping therapy in treating different kinds of diseases.

## Cupping Therapy for Treatment of Acute and Chronic Pain Conditions

Chronic pain conditions constitute a big challenge to physicians being difficult to treat despite a long list of drug classes currently used to treat pain. The etiology of chronic pain is variable and diagnosis of pain differs widely. Chronic pain occurs in rheumatoid arthritis (RA), fibromyalgia, chronic non-specific pain [2]. Pharmacological treatment modalities for pain include non-steroidal anti-inflammatory drugs, steroids and up to the use of opioids [3]. In many cases, patients cannot tolerate treatment side effects that may force them to discontinue treatment. Searching for potentially more effective, economic and less toxic lines of treatment seems mandatory. Cupping therapy may be a solution for suffering faced in many diseases manifested by pain. Reviewing the literature for cupping therapy revealed that it can relieve pain of lumbar disc herniation, herpes zoster, cervical spondylosis [4], RA [5], brachialgia paraesthetica nocturna [6], CTS [7], acute gouty arthritis [8], fibrositis [9], fibromyalgia [10-13], persistent nonspecific low back pain [14], chronic non-specific neck pain [15-17], chronic osteoarthritis [18], acute trigeminal neuralgia [19], headache and migraine [20]. For proper worldwide recognition of cupping therapy, improvement of disease conditions on cupping therapy needs proper scientific interpretation for scientific mechanisms underlying benefits of cupping therapy.

## Mechanisms and Theories about How Cupping Therapy Works

The mechanisms of action of cupping therapy need to be elucidated. Many questions arise from time to time about the exact role of cupping in treating diseases and medical conditions that seem resistant to current treatment modalities. Many theories exist to explain benefits of cupping therapy. We will discuss briefly some of them to get a complete idea about how cupping therapy works.

### Chinese theory for cupping therapy

The concept and theory about mechanism of cupping therapy according to the Chinese theory need revision in light of modern medical scientific knowledge. Practitioners of cupping therapy in traditional Chinese medicine (TCM) may believe that diseases are caused by stagnation or blocking the source of vital energy of life (Qi). They believe that cupping therapy works by unblocking Qi and restoring correct balance to regain its flow [21]. According to the traditional Chinese medical sexology, female gives Yin (female Qi) and receives Yang (male Qi), while male gives Yang and receives Yin. Both the Yin and Yang modalities of Qi are actively present in all males and females [22]. It was explained that cupping therapy can remove the wind, cold, dampness and stagnant blood, especially when cupping therapy was combined with acupuncture [23]. Laser acupuncture combined with cupping in the painful area were thought to facilitate the flow of Qi in meridians according to Arndt-Schulz Biological Law [24].

Some scientists in the western world follow this theory e.g. Ilkay Chirali described ten methods of cupping therapy in his book entitled (Traditional Chinese Medicine Cupping Therapy). The ten cupping methods mentioned by the author included weak/light cupping, medium cupping, strong cupping, moving cupping, needle cupping, moxa/hot needle cupping, empty/flash cupping, full/bleeding cupping, herbal cupping and water cupping [25]. The author mentioned some details

about each type of cupping therapy and attributed the mechanisms of cupping therapy to be due to inducing changes in Qi (energy source), Xu (deficient blood), Wei Qi (defensive energy) and other concepts according to the Chinese theory. For example, fibromyalgia, in TCM, is mainly caused by emotional stress and depression, which affect the liver. Stagnation of Qi activity leads to stasis of blood that causes pain. The principle of treatment is regulating the Qi and blood with dispelling cold and removing damp [26,11].

However, the concepts of energy source and stagnant or deficient blood seem not to be in line with the basic scientific medical concepts. To discuss that from the medical and scientific point of view, it is worth saying that the source of energy in living cells come mainly from mitochondrial oxidative phosphorylation reactions in all body cells containing mitochondria. Added to that, glucose oxidation (glycolysis) is a cytoplasmic source of energy in body cells [27-31] and its importance increases in cells lacking mitochondria as red blood cells (RBCs) and in cells having few numbers of mitochondria as neutrophils [32]. Fatty acid oxidation and ketone bodies oxidation are other mitochondrial sources of energy [33]. Energy production in mitochondria in cancer cells does not follow this rule as cancer cells are having mitochondrial mutations and are characterized by glycolytic phenotype in getting energy. Catabolism of glucose in cancer cells provides most of their energy source (ATP) and ends with production of lactate (Warburg effect) that is extruded outside cells [27]. In previous publications by El Sayed et al., targeting energy glycolytic pathways selectively killed cancer cells and spared normal cells [28-31]. Energy sources in cells do not seem to have any relation with cupping therapy. No scientific reports mentioned that cupping therapy can affect glycolysis or mitochondrial pathways for energy production.

### Mechanisms of cupping therapy according to Hong et al.

Hong et al. reported that cupping therapy works via creating specific changes in local tissue structures as a result of local negative pressure in the cups used which stretches the nerve and muscle causing an increase in blood circulation and causing autohemolysis [35]. When investigating the mechanisms proposed by Hong et al., it may be accepted to mention that local negative pressure may affect tissue structure and increase blood circulation but this is not enough to explain benefits of cupping therapy in treating cellulitis, migraine, headache, hypertension, CTS and others. In addition to that, is autohemolysis beneficial for therapeutic benefit in previously mentioned diseases? The answer is negative. Hong mechanisms partially succeeded in explaining therapeutic effect of cupping therapy.

### Mechanisms of cupping therapy according to Gao et al.

Gao et al. suggested that putting cups on selected acupoints on the skin produces hyperemia or hemostasis which results in a therapeutic effect [4,36]. However, this seems not enough to explain therapeutic benefits of cupping therapy as regard effect of cupping therapy in treating RA, CTS, cellulitis and others.

### Reported mechanisms for analgesic effects of cupping therapy

Many possible mechanisms were reported to explain cupping-induced analgesia when wet cupping therapy (WCT) was used in treatment of CTS. Cupping therapy may induce deformation or injury to the skin leading to stimulation of A $\beta$  fibers in the painful region and distal skin regions and stimulation of inhibitory receptive fields of the multi-receptive dorsal horn neurons at the level of the spinal cord. In addition, cupping therapy may simulate special naturopathic setting leading to relaxation and comfort of the patient [37,7].

WCT-induced analgesia may be similar to the effect of acupuncture and occurs via segmental, extra-segmental and central regulatory action. However, acupuncture differs from WCT as regard their mechanisms of action [38]. Moreover, WCT-induced skin laceration creates a vacuum on the skin and draws out a small amount of blood [39]. Local damage of the skin and capillary vessels (induced by WCT) may cause a nociceptive stimulus that stimulates diffuse noxious inhibitory control [40] in addition to the affective component of chronic musculoskeletal pain [41], which may relieve pain associated with the affective component through the limbic response [42]. Therefore, the tactile stimulus of WCT may be responsible for the analgesic effect.

Cupping therapy enhances blood circulation, treats congestion and stops the inflammatory extravasations (escaping of some body fluids e.g. blood) from the tissues [25,43]. WCT may affect the autonomic nervous system and help to reduce pain [25,43]. However, although previously mentioned explanations may explain analgesic effect of cupping therapy, it is still not enough to explain how cupping therapy itself treats so many diseases with different etiologies and pathogenesises.

### Taibah theory (by Salah M. El Sayed) for scientific mechanisms of cupping therapy e.g. Al-hijamah (WCT of prophetic medicine)

Human body is kept under physiological homeostasis by the harmony of body systems and organs. Disease etiopathogenesis occurs against physiological homeostasis. Disease pathophysiology varies according to the etiology of each disease and its effect on disturbing body homeostasis. The beauty of cupping therapy comes from the fact that cupping therapy is an excretory form of therapy not an introductory one in which cupping removes blood and tissue fluids mixed with potentially harmful substances. We report here a novel simple theory to explain scientific mechanisms that govern the process and therapeutic benefits of WCT. WCT seems to be related in principle to the scientific principles governing excretory functions of the kidney to the extent that WCT may be regarded as an artificial kidney that performs skin capillary filtration and size-dependent excretion of particles at pressures higher than filtration pressures in renal glomeruli.

While excretion through kidney is limited to hydrophilic materials [44], cupping therapy can excrete hydrophilic and hydrophobic materials as lipoproteins [45] and enhance the natural excretory role of the skin. Differences and similarities between excretions through kidneys versus WCT are mentioned in table 1. We hypothesize also that WCT may be also related to surgical principles beyond evacuation of an abscess with some similarities and differences (Table 2). Treatment using cupping therapy keeps human body away from a long list of undesired side effects and possible drug-drug interactions of therapeutic drugs. Searching for scientific principles of WCT urged us to propose a new mechanism to explain scientific and medical bases of cupping therapy, Taibah theory. As WCT includes both dry cupping therapy and skin puncturing, first part of Taibah theory gives scientific principles of dry cupping therapy.

Taibah theory states that: Al-hijamah is WCT of prophetic medicine (Arabic in origin). Al-hijamah includes all steps (and consequently similar or better therapeutic benefits) of both Chinese dry cupping therapy and WCT altogether. Al-hijamah is related in principle to the scientific mechanisms underlying abscess evacuation and fluid filtration at renal glomeruli, where a pressure-dependent excretion of harmful substances and CPS occurs. CPS include both disease-causing substances and disease-related substances resulting during disease pathogenesis.

Al-hijamah is a minor surgical excretory procedure, where negative pressure (suction force) applied to skin surface using cups creates skin upliftings (gradually increasing in size due to viscoelastic nature of the skin) inside which local pressure correspondingly decreases (Boyle's law) around capillaries. This causes increased capillary filtration, local collection of filtered fluids, lymph and interstitial fluids and their retention inside skin upliftings. This dilutes chemical substances, inflammatory mediators, nociceptive substances, bathes nerve endings in collected fluids and breaks tissue adhesions causing decreased pain (Taibah theory for dry cupping therapy). On removing the cups, dramatic increase in skin blood flow occurs (reactive hyperemia).

	Excretion through kidney	Excretion through wet cupping therapy (percutaneous route)
<b>Route and function</b>	Natural (does not need skin scarifications)	Artificial (needs skin scarifications)
<b>Steps</b>	Filtration (from glomerulus to Bowman's capsule), secretion, reabsorption and excretion.	Filtration of capillary blood, cleansing of interstitial spaces and excretion of excess fluids and wastes (CPS).
<b>Capillary types</b>	Non-sinusoidal fenestrated capillaries with open 'non-diaphragmed' fenestrae [46].	Non-sinusoidal fenestrated blood capillaries with diaphragmed fenestrae [46].
<b>Capillary pore sizes</b>	15 nm [46]. Diameter of fenestrae is 65 nm	6-12 nm [46]. Diameters of fenestrae range between 60 and 80 nm
<b>Material excretion</b>	Depends on molecular size and hydrophilicity (smaller water soluble crystalloid substances as organic acids are excreted, while colloids as plasma proteins are not).	Both crystalloids and colloids e.g. $\beta$ -lipoprotein (Molecular weight: 1,300,000) can pass through the skin capillaries into the interstitial fluid [145-147] then cupping therapy opens the skin barrier and enhances natural excretory role of the skin.
<b>Filtration and excretion forces</b>	Controlled by glomerular capillary hydrostatic pressure, osmotic pressure of plasma proteins, permeability, and osmotic solute gradients.	Negative pressure of cupping, capillary hydrostatic pressure, osmotic pressure of plasma proteins and permeability.
	(10 mm Hg) out [144] continuously working	(163 to 433 mmHg) Out i.e. (16-43 times more than in renal glomeruli). Short time (minutes)
<b>Filtrate</b>	Primary urine (Mainly water+electrolytes) Most water will be reabsorbed.	Interstitial fluid+filtered fluids from blood capillaries+some traumatic capillary blood
	Water-like	Blood-like
<b>Substances candidate for excretion</b>	hydrophilic	Hydrophilic and hydrophobic e.g. lipoproteins as LDL.
<b>Requirements for excretion</b>	Patent urinary pathways	Skin incisions in wet cupping therapy+cupping pressure
<b>Major function</b>	. Clears blood from metabolic waste products.	. Clears interstitial spaces and blood from CPS, accumulated waste products, biological and chemical substances.
	. Acid-base balance	. Has therapeutic and preventive role in many different diseases.
	. Hematopoietic role	
<b>Reabsorption</b>	occurs	Permanent excretion

**Table 1:** Differences between excretion through renal glomerular filtration and excretion through wet cupping therapy.

	<b>Abscess incision and evacuation</b>	<b>Excretion through wet cupping therapy</b>
<b>Mechanism of action</b>	Artificial excretion through skin	Artificial excretion through skin
	Pyogenic inflammation is localized into abscess cavity by activity of immune system.	CPS, Cellular byproducts, metabolic waste products, free radicals, chemical and biological substances are discharged to the tissue fluids and blood.
<b>Purpose of incision</b>	To drain pus, necrotic, liquefied tissues and toxins	To excrete CPS, byproducts, waste, chemical, biological substances and others.
<b>Result after intervention</b>	Subsidence of inflammation	Subsidence of pathology.
<b>Pressure applied</b>	Compression pressure to evacuate abscess cavity and to break pus sockets	Vacuum negative pressure to excrete CPS and collected tissue fluids across skin incisions then to filter intravascular fluids from CPS through capillary walls to the empty interstitial spaces then to outside.
<b>Site of skin incision (s)</b>	At the most prominent point of abscess	- At tender points for local therapeutic effect. - At back of neck and other sites for general preventive and therapeutic uses.
<b>Importance</b>	Absolutely necessary to treat localized pyogenic inflammation (abscess).	Highly recommended for prophylaxis and is a therapeutic line of treatment for many diseases
<b>Associated medications</b>	Broad spectrum antibiotics	No need (antibiotics are advisable)
<b>- Effect of neglect (if not done)</b>	Toxemia and septicemia	. Gradual accumulation of harmful substances.
<b>- Complications of procedure</b>	Not serious	Not serious

**Table 2:** Differences between excretion through abscess evacuation and excretion through wet cupping therapy.

Scarifications of surface of skin upliftings opens skin barrier for evacuation of fluids with CPS and prevents their absorption at venous capillary end. Immediate second cupping pressure is transmitted through skin incisions to create a pressure gradient and a traction force across the skin and capillaries leading to excretion of collected interstitial fluids (including lymph) with CPS, filtration of capillary fluids containing CPS, bleeding at puncture sites and increased release of endogenous opioids (analgesic effect).

Cupping therapy increases innate and acquired immunity (skin wounding effect), hemolyzes old RBCs against high-pressure gradient and enhances natural excretory functions of the skin.

Old hemolysed blood cellular fragments, molecules and particles smaller than capillary pore sizes selectively pass through capillary pores under suction pressure effect, while intact blood cells (larger than sizes of pores and fenestrae of skin capillaries) do not.

In the cupped area, traumatized capillaries may bleed. Therapeutic benefits of WCT is not related to the amount of blood drawn out but to the amount of excreted CPS. WCT benefits from the vasodilator, antimicrobial, angiogenic and wound healing effects of released nitric oxide (NO).

WCT-induced fluid and CPS excretion, negative pressure suction and NO may help in dilating local blood capillaries. This improves microcirculation, increases capillary permeability, increases drainage of excess fluids, increases lymph clearance and flow, decreases absorption at venous end of capillaries, increases fluid filtration at both arterial and venous capillary ends, increases fluid excretion (filtered fluids and interstitial fluids) causing increased clearance of blood, plasma, lymph and interstitial spaces.

All that lead to decreasing interstitial fluid pressure, decreasing capillary venous return, decreasing venous pressure, decreasing peripheral vascular resistance, enhancing velocity of blood flow, treating blood congestion, improving blood and lymphatic capillary circulations and resolution of tissue swelling (due to removal of CPS, noxious substances, prostaglandins and inflammatory mediators).

All these effects may improve oxygen supply, tissue perfusion and cellular metabolism, preserve underlying and remote tissue structures, modulate angiogenesis, relieve muscle spasm, restore balance of neuro-endocrine system, improve neurotransmission, improve affective component of pain, exert pharmacological potentiation to conventional treatments and restore physiological homeostasis. Health

and therapeutic benefits after Al-hijamah may include improvement of general condition, excretory benefit (of CPS and noxious substances), immunological benefit, pharmacological benefit (potentiating and facilitating therapeutic effects of drugs through removing CPS), neurological benefit (improving headache), detoxification benefit, metabolic benefit (improving cellular perfusion), nutritional benefit (decreasing LDL and cholesterol), cosmetic benefit (breaking adhesions, resolving inflammation and swelling), hemostatic benefit, hematological benefit (blood clearance of CPS and old hemolyzed blood cells), hemodynamic benefit (improving local capillary circulation), angiogenic benefit, psychological benefit (secondary to all benefits and due to improvement of affective component of pain) and treatment of disease predisposing factors. Al-hijamah should be done whenever excess CPS (solutes) or fluids are to be excreted to gain disease cure or improvement. This covers also all diseases that benefit from Chinese dry cupping therapy and/or WCT taking into account the other possible therapeutic benefits of Al-hijamah).

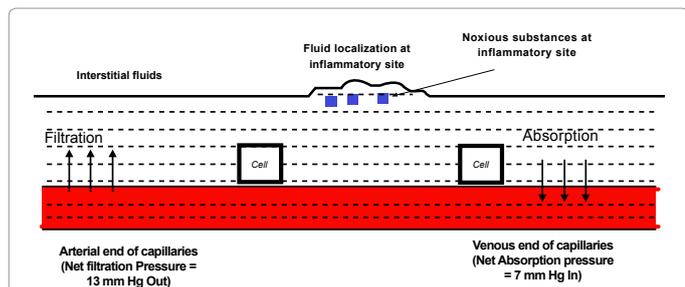
Salah's theory for WCT is named Taibah theory (named after Taibah city, Al-Madinah Al-Munawwarah, city of Prophet Mohammad peace be upon him). In light of Taibah theory, prophetic method of WCT (Al-hijamah) can be defined as a minor surgical excretory procedure that creates superficial skin scarifications to open skin barrier and create a pressure gradient and a traction force across the skin and underlying capillaries to drain interstitial fluids and enhance blood clearance and waste excretion through skin.

From Taibah theory, it can be concluded that WCT works through inducing local fluid collection in skin upliftings that comes out through inducing skin scarifications leading to decreased interstitial fluid pressure and clearance of interstitial spaces. This causes a pressure gradient and traction force across the walls of blood and lymphatic capillaries in the cupped area to drain solutes and fluids to interstitial spaces then through skin scarifications to outside. This enhances blood circulation and lymph flow and directs filtered fluids (including lymph) to the cupped area with further clearance of blood and lymph in the short time period during which negative suction is applied. This may help to regain homeostasis in human body (Figures 1-2).

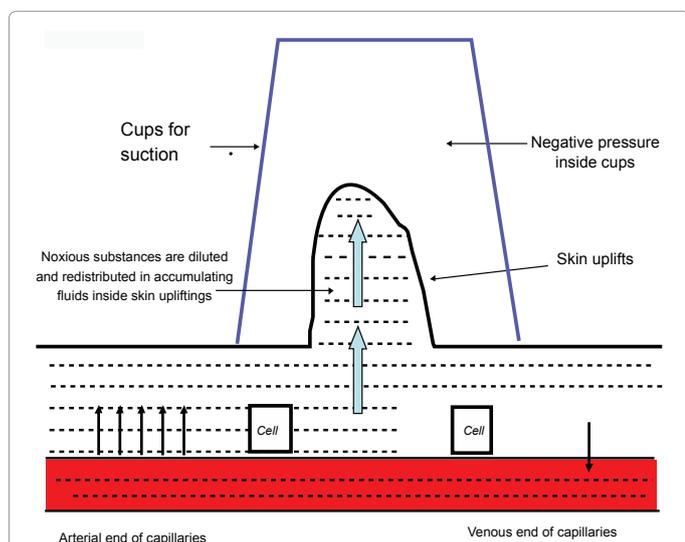
Unless there is a contraindication for any of the cupping steps, Al-hijamah may be regarded as a beneficial artificial percutaneous route of excretion. Whenever excess fluids, organic substances or solutes are to be drained, evacuated or excreted, WCT may be beneficial.

### Scientific Evidences in Favor of Taibah Theory

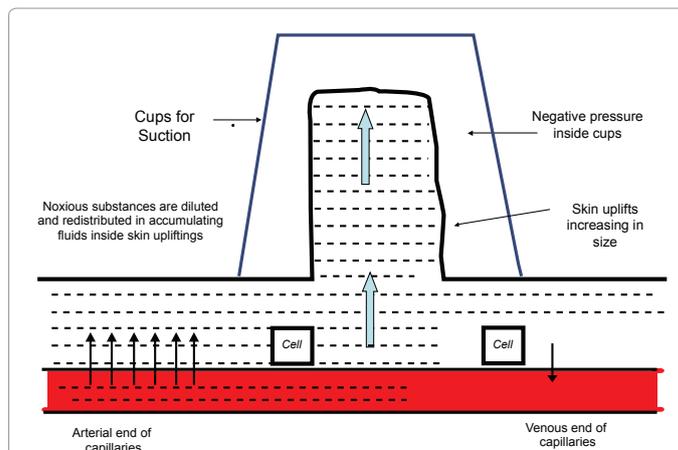
Careful analysis of scientific facts in histology and physiology of



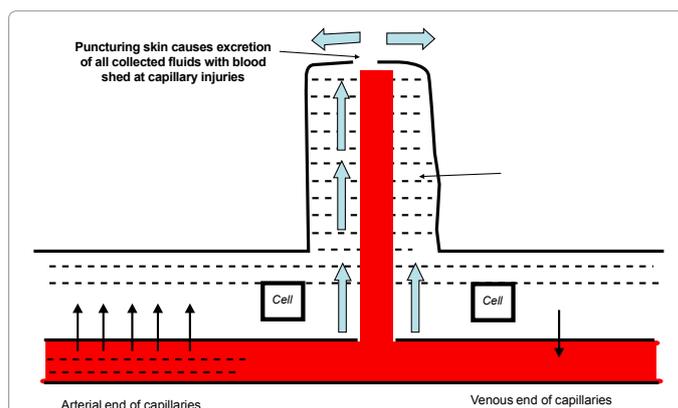
**Figure 1a: Illustration of Taibah theory for cupping therapy. (A) Fluid localization at sites in disease conditions.** Noxious substances (CPS) are localized beneath the skin surface in contact with tissue fluid, which is in continuous exchange with capillary blood. Tissue fluid is filtered at arterial end of capillaries and is absorbed at venous end of capillaries.



**Figure 1b: First step of Al-hijamah (Dry cupping therapy):** On application of negative suction pressure, viscoelastic nature of the skin causes sucking of skin inside cups creating skin uplifting inside which interstitial fluids start to accumulate. Filtration increases at arterial end of capillaries; while absorption decreases at venous ends due to movement of fluids to skin upliftings.



**Figure 1c: More accumulation at end of the step of Al-hijamah (Dry cupping therapy):** Viscoelastic nature of skin causes sucking of skin inside cups leading to increased size of skin upliftings inside which pressure decreases (Boyle's law) causing more fluid (with CPS) filtration and more accumulation of interstitial fluids (with CPS). Filtration increases at arterial ends of capillaries; while absorption decreases at venous ends due to movement of fluids to skin upliftings causing clearance of blood and cleansing of interstitial spaces.



**Figure 1d: Second step of Al-hijamah (puncturing):** On scarifying skin, fluids collected inside skin upliftings start to get out mixed with blood resulting from capillary injuries causing more clearance of blood from CPS.

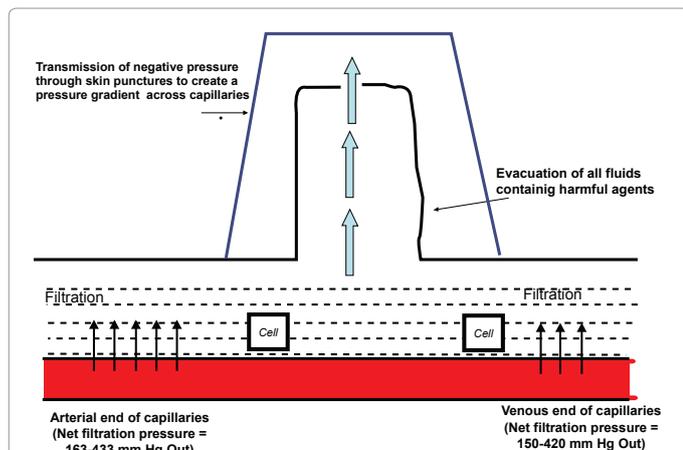
capillary circulation and the literature support Taibah theory for WCT, as we will review here.

## 1. WCT Causes a Pressure-Dependent and Size-Dependent Excretion of CPS

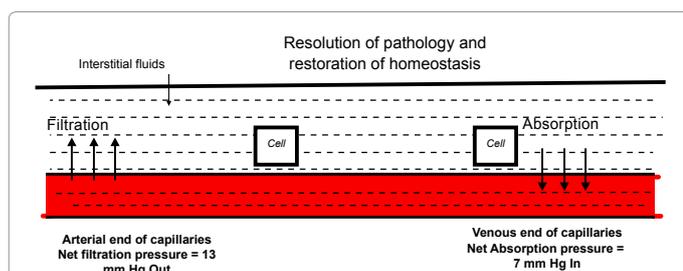
Skin capillaries include both non-fenestrated blood capillaries with loose junctions (pore size is about 5 nm) and non-sinusoidal fenestrated blood capillaries with diaphragmed fenestrae (physiological upper limits of pore sizes range between 6 and 12 nm). Capillary skin fenestrae may reach 60-80 nm in size. Stretching of pores of skin capillaries was reported to increase pore and fenestral size to increase permeability through skin capillaries. Vessels located in close proximity to the epidermis exhibit endothelial fenestrations along their proximal margins. In vessels away from the epidermis, fenestrations are not apparent [46]. Since endothelial fenestration is an anatomical property related to rapid material exchange, this confirms pressure-dependent and size-dependent excretory functions of Al-hijamah. This also confirms that skin scarifications done during Al-hijamah should be so superficial to allow the process to benefit more from the superficial

location of the fenestrated skin capillaries. Compared with skin capillaries, kidney glomerular capillaries (non-sinusoidal fenestrated capillaries with open non-diaphragmed fenestrae) have slightly wider pores (15 nm) [46], which confirms the size-dependent filtration of blood through skin capillaries (in Taibah theory) leading to plasma filtration and excretion of CPS soluble in plasma. Added to that is the strong negative pressure used during WCT (strong filtration force) that is stronger than filtration pressure at glomerular capillaries.

The viscoelastic nature of human skin confirms that it is not plane and allows skin to be modeled in simulation studies where skin can be sucked up into the inside of cups to a certain extent [21,37]. Sucking skin into the inside of cups depends on the amount of pressure applied, point of skin at which cup is applied, subcutaneous tissue and size of cups. Suction pressure (negative pressure) in cupping therapy leads to fluid collection inside skin upliftings then excretion of larger amount of fluids through skin scarifications more than the amount that can be produced without suction. Progressive increase in size of skin upliftings



**Figure 1e: Third step of Al-hijamah (second cupping):** On applying pressure suction again to skin, negative suction pressure is transmitted through skin incisions causing all fluids (with CPS) collected inside skin upliftings to start to get out mixed with blood resulting from capillary injuries till emptying of all collected fluids. As there is a high pressure gradient due to added cupping pressure (filtration force) at both capillary ends (arterial and venous ends of capillaries), fluid filtration occurs at both capillary ends causing more clearance of blood.



**Figure 1f: Resolution of pathology and restoration of homeostasis.** Noxious substances beneath skin surface are removed and tissue swelling is resolved. New tissue fluid is formed through filtration at arterial ends of capillaries after removal of previous tissue fluids containing noxious substances (CPS). Again, tissue fluid is filtered at arterial end of capillaries and is absorbed at venous end of capillaries. Physiological homeostasis is now restored after wet cupping therapy.  
In: fluid absorption to the inside of capillaries. Out: fluid filtration to the outside of capillaries.

around capillaries can decrease pressure around capillaries (Boyle's law) leading to more capillary filtration and excretion of CPS (in agreement with Taibah theory) that confirms benefits of the pressure effect in cupping therapy.

Moreover, the negative pressure applied at the skin surface during cupping therapy is variable in strength according to the method of production of this negative pressure. Huber et al. reported that large pressure differences could be obtained when using different methods for inducing negative pressure. Huber et al. reported that mean pressure produced was  $-200 \pm 30$  hecta Pascal (hPa) when using 2 cm flame,  $-310 \pm 30$  hPa with 4 cm flame,  $-560 \pm 30$  hPa with burning alcohol soaked cotton swab and  $-270 \pm 16$  hPa with rubber balloon. The pressure produced through rubber balloon was the easiest technically, moderate (not too high or too low) and was the most reproducible on repeating cupping practice as evidenced by reduction of the standard deviation by a factor of 2 compared to the flame methods.

When WCT is done across the skin barrier, negative pressure

produced in previously mentioned methods was  $(-200$  to  $-560$  hPa) [37] which is equivalent to  $(-150$  to  $-420$  mmHg). This negative pressure at skin surface creates skin upliftings inside which collection of interstitial and filtered fluids take place. This decreases absorption at venous ends of capillaries (fluid moves to skin upliftings) and increases filtration at arterial ends. This confirms the pressure-dependent excretory role of WCT (Taibah theory). Adjustment of the suitable pressure needed can be achieved through selecting the best pressure method. No need for very high suction pressures if capillary rupture may occur as excretion of CPS can better be achieved through capillary blood filtration than through bloodletting.

As the negative suction pressure during cupping therapy is much higher than the net filtration pressure at the arterial side of the capillaries (both are filtration forces pushing fluids from inside capillaries to the interstitial spaces) and also much higher than the net venous pressure (absorptive pressure) at the venous side of capillaries as indicated in the normal pressure values at capillary ends [47] as summarized in table 3, WCT increases capillary filtration at both capillary ends (in agreement with Taibah theory). This becomes obvious on puncturing skin surface and opening skin barrier where pressure gradients across skin surface and capillaries occur. Negative pressure will be a filtering force added to the hydrostatic pressure at both arterial and venous ends of capillaries to enhance filtration at both ends of capillaries (arterial and venous ends) leading to continuous filtration at both ends of capillaries and further clearance of blood and plasma.

## 2. Intact Blood Cells are not Filtered by Al-hijamah-Induced Pressure Filtration

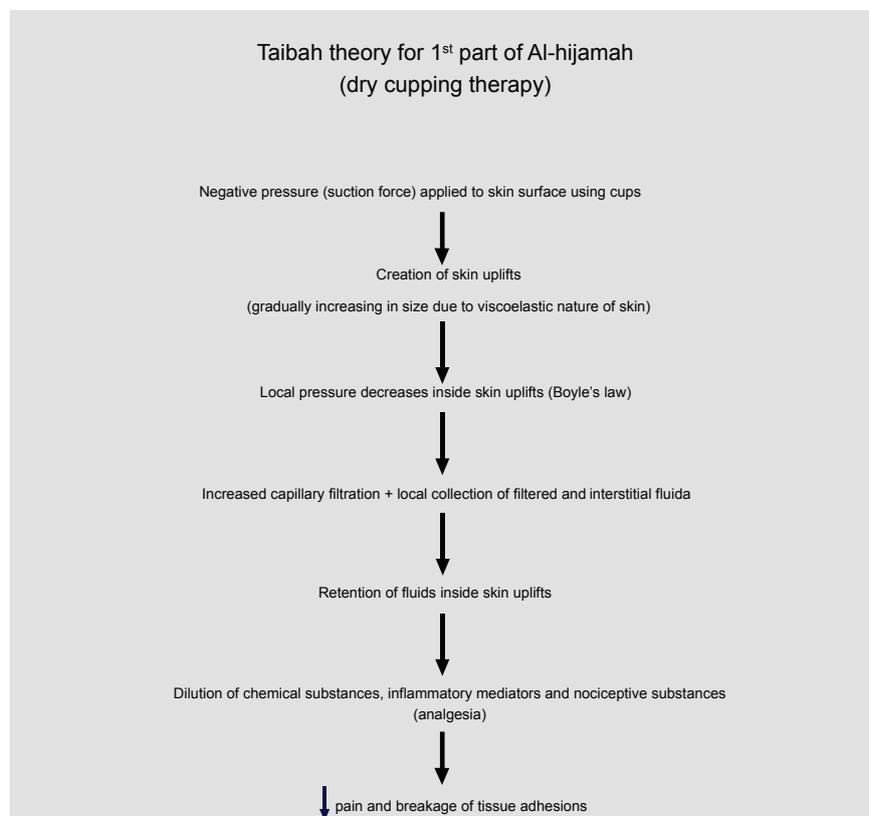
Excretion through WCT is selective. It depends on strength of pressure applied, time allowed, number of cups applied, frequency of cupping therapy and size of capillary fenestrae and pores. As diameter of pores and fenestrae of skin capillaries (12 nm and 60-80 nm, respectively) is relatively near to diameter of pores and fenestrae of glomerular capillaries (15 nm and 65 nm, respectively) [46], only small particles in nanometer range will be filtered through skin capillaries (percutaneous route) and then excreted. RBCs, WBCs and platelets have sizes in micrometer range [48] more than size of capillary fenestrae (in nanometer range) and therefore can never leak through capillary pores. Hemolysed blood cellular fragments and old hemolyzed cells may pass through capillary pores. Intact blood cells that may be present in cupped blood must come through traumatized capillary points. Red color of cupped blood is due to both hemolyzed and intact cells and liberated hemoglobin from hemolyzed RBCs. Based on that, optimization of the cups size, cups number, time factor, pressure factor and anatomical sites for cups application will improve therapeutic outcomes of WCT.

In addition, filtration in WCT may be stronger than glomerular capillary filtration due to higher pressure in case of cupping therapy (16-43 times higher pressure in WCT more than net pressure at glomeruli) (Table 3).

In addition, opening skin barrier increases the inherent excretory role of the skin to excrete lipids and hydrophobic sebaceous substances as evidenced by the report that skin guards against metabolic syndrome [49] and the report that WCT decreased serum lipids profile levels of hyperlipidemic patients [45].

## 3. Some Loss of Venous Blood Occurs on Scarifying Skin During Al-hijamah

Cupped blood shed out during Al-hijamah showed decreased levels of blood constituents and cells in comparison with venous blood



**Figure 2a: Summary of Taibah theory for explaining the mechanisms of cupping therapy.** (A) Taibah theory for explaining first step of Al-hijamah (dry cupping therapy).

values [50-51]. This may be due to dilution of blood shed out at skin puncture sites with the added collected interstitial and filtered fluids. For example, blood shed out during cupping therapy showed highly significant decline in number of WBCs, RBC, platelets, monocytes and granulocytes. Also, there was a significant decrease in hemoglobin level, hematocrit value and mean cell hemoglobin concentration [50-51]. This confirms that venous blood (undiluted with added fluids) is different from blood shed during WCT (diluted with added fluids) in agreement with Taibah theory.

#### 4. Al-hijamah has Analgesic and Immunological Functions

During WCT, skin is punctured. It was reported that injury to the skin leads to release of  $\beta$ -endorphin (endogenous analgesic opioid) and adrenocortical hormones into the circulation. Endothelin-1 is a pain mediator synthesized by normal skin keratinocytes upon skin injury and acts on endothelin-A receptors. Endothelin-1 can produce analgesia via acting also on endothelin-B receptors leading to the release of  $\beta$ -endorphin from keratinocytes and the activation of G-protein-coupled potassium channels linked to opioid receptors on pain receptors [52-56]. Also, the outer root sheath of the anagen hair follicles of skin and dermal fibroblasts [53] mainly produces  $\beta$ -Endorphin. Both  $\beta$ -endorphin and adrenocortical hormones could be helpful in blocking inflammation in arthritis [54]. Moreover, skin nerve endings are bathed in collected fluids inside skin upliftings, which may reduce their stimulation (analgesic effect). Based on that, skin injury (as skin scarifications during WCT) has analgesic effect through release of endogenous opioids [52-56].

In addition, skin manipulation by needles and electric stimuli causes

release of endogenous opioids and neuropeptides e.g. enkephalin, beta-endorphin and endomorphin in the central nervous system (analgesic effect), while electric stimulus of 100 Hertz selectively increases the release of dynorphin [57]. Based on that, WCT-induced analgesic effect may act using the same pathway.

Moreover, WCT exerts immunomodulatory and regulatory effects on the immune cells e.g. WCT was reported to increase number of natural killer (NK) cells (innate immunity) [5]. In addition, substance P was reported to play a role in peripheral inflammatory responses and pain genesis. Recent evidence from animal models indicates that antagonists of substance P can block peripheral inflammatory responses as well as nociception (pain) associated with inflammation [58]. Based on that, dilution of substance P and other inflammatory mediators in collected fluids inside skin upliftings may decrease pain sensation.

Skin scarifications (as that done during cupping therapy) stimulate immune system through the components of the innate immune response in the skin where 3 antimicrobial peptides: the cathelicidins, defensins, and dermcidins act as antimicrobials by enhancing activity of the innate immunity, humoral immunity, cell-mediated immune response and directly inhibiting pathogen growth [59]. Based on that, WCT has an important immunological benefit.

#### 5. Al-hijamah Enhances Excretory Skin Functions and Clears Interstitial Spaces

WCT works as an excretory procedure at the skin and interstitium. The interstitium is not a passive fluid reservoir as its connective tissue cells and extracellular matrix have a role in the control of pressure of the interstitial fluids e.g. the interstitium has a critical role in the

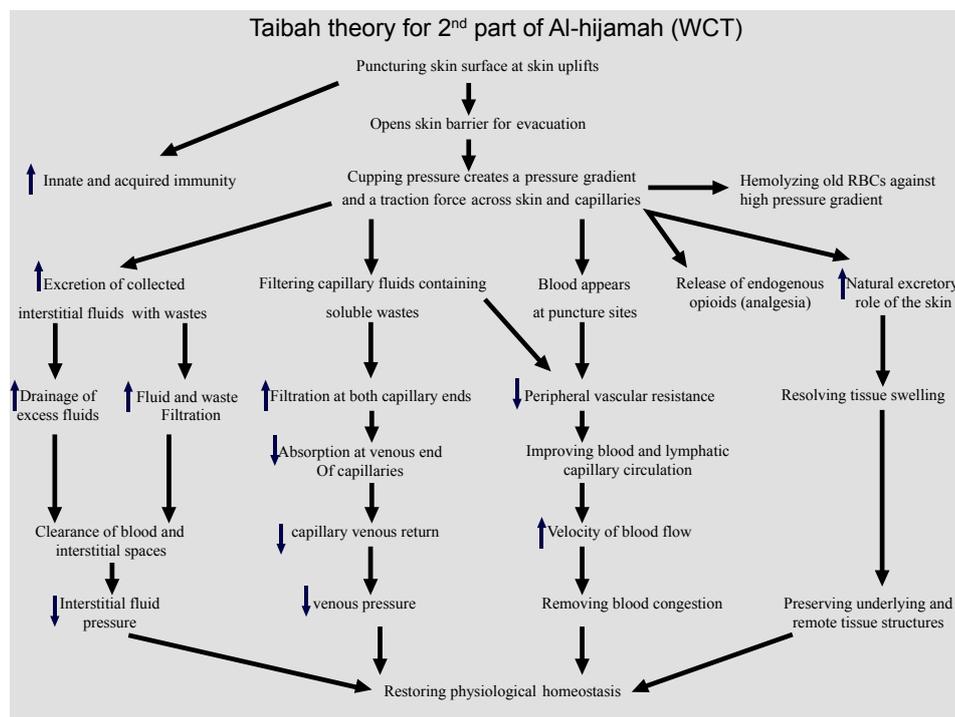


Figure 2b: Taibah theory for explaining second part of Al-hijamah (WCT).

Type of pressure	Arterial end of capillaries	Venous end of capillaries
<b>Hydrostatic pressures (mm Hg)</b>		
. Blood hydrostatic pressure	30 mmHg Out	10 mmHg Out
. Interstitial hydrostatic pressure	3 mmHg Out	3 mmHg Out
	<b>33 mmHg Out [47]</b>	<b>13 mmHg Out [47]</b>
<b>Colloid osmotic pressures (mm Hg):</b>		
. Of blood	28 mmHg In	28 mmHg In
. Of tissue fluids	8 mmHg Out	8 mmHg Out
<b>Net Absorption pressure =</b>	<b>20 mmHg In [47]</b>	<b>20 mmHg In [47]</b>
<b>Net pressure force = net hydrostatic pressure – net absorption pressure (mm Hg) (in absence of pressure of cupping therapy)</b>	<b>13 mmHg Out (filtration force)</b>	<b>7 mmHg In (absorption force)</b>
Cupping therapy pressure force (mm Hg) (= filtration force)	(150 to 420 mmHg) Out (filtration force) [37]	(150 to 420 mmHg) Out (filtration force) [37]
<b>Net pressure force (after adding cupping therapy)</b>	<b>(163 to 433 mmHg) Out</b>	<b>(143 to 413 mmHg) Out</b>

Table 3: Pressure forces governing tissue fluid filtration and absorption with and without wet cupping therapy.

rapid development of edema in burns and in the induction of initial swelling in inflammation [60]. Based on that, WCT-induced negative pressure can benefit the interstitium through resolving edema and tissue swelling.

The skin is the largest organ in human body and has an important excretory function. Skin can degrade, inactivate, biotransform, detoxify and eliminate numerous drugs, chemicals and endogenous toxic compounds through its drug-metabolizing enzymes [61-63], antioxidant systems, ROS-scavenging system [64] and excretion through sweat glands [65-69]. Based on that, WCT-induced openings of the skin barrier may help further excretion of reactive oxygen species (ROS), free radicals and the above-mentioned substances and improve the natural excretory functions of the skin (in agreement with Taibah theory). As an evidence for the important excretory functions of the

skin, severe skin burns cause permanent skin structural tissue damage that may be associated with abnormal metabolism in the form of long lasting insulin resistance, endoplasmic reticulum stress response, increased metabolism, increased cortisol, increased catecholamine and increased cytokines [70-72]. Moreover, impaired cutaneous vasodilatation and sweating are found in grafted skin [73]. This confirms the excretory importance of WCT as this treatment modality opens skin barrier and helps excretion of all that matter.

Moreover, sweat glands of human skin (eccrine sweat glands) measure about the weight of one kidney (about 100 g) and can excrete numerous drugs, metals, xenobiotics [65-67], endogenous chemical and biological substances e.g. neurotransmitters, cytokines, heavy metals and sterols [68,74-76]. Therefore, it can be concluded that decreased skin functions due to burn injuries may increase the

risk of accumulation of toxic substances in the body. Based on that, WCT-induced skin incisions become important to facilitate excretion through the skin and its importance increases in presence of skin damage. In addition, WCT becomes more important when complicated skin problems e.g. complicated burns occur in full-thickness skin as evidenced by the report by Liu et al. who reported that the expression of enzymes metabolizing xenobiotics, drugs and ROS scavenging enzymes was not detected in the full-thickness burnt rat skin. Burn causes increased generation of free radicals as hydrogen peroxide [76]. Based on that, WCT opens skin barrier and may cause relief of that harmful stress.

## 6. Skin Histology is Ideal for Practicing Al-hijamah

Histologically, human skin is composed of epidermis and dermis. The epidermis is the outermost, cellular and nonvascular layer of the skin having thickness ranging from 0.07 mm to 0.12 mm (0.8 to 1.4 mm in the palms and soles). The epidermis is impermeable to water and has protecting barrier functions against physical, ultraviolet injury, chemicals and microbial penetration [77-78]. The epidermis can tolerate mechanical stress (as that during cupping therapy) by continuous turnover through migration of the cells originating at the basement membrane to the above layers [78].

The dermis is the second layer of the skin and represents the vascular connective tissue matrix that interacts with the epidermis. Dermis is strong, elastic, thin (1 mm to 3 mm) and can store water. Based on that, depth of human skin is relatively thin (average 2 mm) and is richly supplied by a network of capillaries [77-78]. This facilitates WCT through that shallow depth of the skin and facilitates blood clearance through filtration of blood circulating in this rich capillary network.

Dermis contains also elastin protein for elasticity, collagen protein for strength, glycosaminoglycans (dermatan sulfate, hyaluronic acid and chondroitin sulfate), which make up the ground substance surrounding the fibrous components that contribute to the viscoelastic nature of skin [77-78]. Dermal cells are fibroblasts, macrophages, mast cells, and leukocytes. Fibroblasts synthesize collagen, elastin, and glycosaminoglycans and help wound healing [79]. Based on that, the above-mentioned factors help skin to afford the negative pressure (suction force) during cupping therapy due to strength (collagen) and elasticity (elastin) of the skin. Fluids excreted with cupping therapy include fluids stored in dermis (in agreement with Taibah theory).

## 7. Al-hijamah may Benefit from NO Production

NO concentration increases in blood plasma following skin punctures in acupuncture in a time-dependent manner. Blood flow in subcutaneous tissue at acupunctured sites also increases and this correlates with the NO increase i.e. acupuncture increases the NO level in treated regions and thereby increases regional circulation. This may explain the analgesic effect of acupuncture [80]. Also, production of endogenous NO was reported to increase after skin injury and in wounds [81]. Based on that, skin scarifications (done during Al-hijamah) may have a similar effect in increasing NO levels.

NO synthesis occurs in human dermal fibroblasts [81] while macrophages were reported to produce NO for prolonged periods after injury [81].

NO synthase synthesizes NO [82]. Both inducible and constitutive isoforms of NO synthase are expressed by human dermal fibroblasts [83]. Expression of NO synthase was reported also in vascular

endothelium [84]. Expression of inducible NO synthase and endothelial NO synthase occurs in macrophages, epidermis, hair follicle, sebaceous gland, fibroblasts (during the healing process of incised skin wounds in mice) and in polymorphonuclear cells in the wound area and peripheral region [84].

NO is critical to wound collagen accumulation, acquisition of mechanical strength and wound healing [85] especially during the inflammatory stages of wound healing. Inhibition of the production of endogenous NO inhibits both leukocyte accumulation and edema formation induced by different mediators of inflammation [83]. NO acts as a neurotransmitter, immunoregulator, vasodilator, anti-proliferative, anti-neoplastic and anti-microbial agent [86] as NO restricts pathogen growth after cutaneous infection [87]. NO plays important roles in cell proliferation, differentiation, apoptosis, angiogenesis, matrix deposition and remodeling [82]. NO influences the behavior of macrophages, fibroblasts and keratinocytes during wound repair [88]. NO stimulates the induction of vascular endothelial growth factor (VEGF) expression in cultured keratinocytes and during cutaneous wound repair [89]. Increased vascular permeability induced by VEGF is mediated by local production of NO and arachidonic acid metabolites other than prostaglandin E<sub>2</sub>, which are most probably produced by inducible NO synthase and cyclooxygenase-2 [90].

Based on that, NO can be produced locally in punctured skin to help wound healing. NO may play a protecting anti-microbial role to skin scarifications during WCT. NO may help in restoring skin physiology after WCT. Also, WCT may affect angiogenesis through NO-induced VEGF pathway.

In diabetes, NO synthesis is reduced in the wound milieu. This may be a factor in diabetes-induced impaired wound healing and there are few therapeutic options to reverse it. The amino acid L-arginine is the only substrate for NO synthesis. Arginine supplementation restored impaired healing in acute wound model by normalizing the NO pathway [91]. However, NO appeared not to affect the impaired inflammatory reaction in diabetes, which was unaffected by NO donor (molsidomine) treatment and ex vivo NO synthesis [92]. Based on that, a promising improvement in healing of diabetic wounds and diabetic foot may be achieved through normalizing the NO pathway by performing WCT.

## 8. Al-hijamah Benefits from the Phenomenon of Reactive Hyperemia

Reactive hyperemia is a protective adaptive phenomenon, which quickly restores blood flow distal to a transient arterial occlusion. NO plays a role in it. Other several mediators are involved e.g. myogenic and metabolic factors, prostaglandins, K<sup>+</sup> ATP channels and adenosine [93]. Vascular compression (as that occurring during application of sucking cups causes a decrease in blood supply to the skin for few minutes resulting in accumulation of vasodilator chemicals. As soon as vascular compression is removed, blood flow to skin dramatically increases causing hyperemia [94]. Based on that, patients may benefit from this reactive hyperemia in filtering more blood and excreting more CPS.

Resting skin blood flow in thermoneutral environments is approximately 250 mL/min. Skin vasodilation increases dramatically with skin warming until skin blood flow can reach 6 to 8 L/min during hyperthermia. Both local sensory nerves and NO may play a role in that [95-96].

However, NO synthase inhibition does not alter the reactive hyperemic response in the cutaneous circulation [97]. Also,

vasodilatation of reactive hyperemia is independent of the central nervous system to a large extent and is related to the metabolic debt and affects the deep as well as the superficial circulation, the arterioles, capillaries and venules [98-102].

Recently, using Doppler flowmetry, there was a 4-fold increase of skin blood perfusion (due to reactive hyperemia) as compared to the level of this parameter at rest [103] i.e. skin blood perfusion increases from 250 to 1000 ml/min, which means that about 10 liters blood will enter skin circulation within 10 minutes (the average duration of WCT). This may allow maximal clearance of blood from CPS. Based on that, WCT may clear an enough proportion of the circulating blood during one session (blood volume is 5-6 liters).

At the back region, post-pressure hyperemia reached a maximum after application of 100 mmHg pressure with no greater hyperemic response on application of higher pressures [104]. Moreover, inflammatory hyperemia occurs at inflammatory sites as a physiological compensation for the abnormal local calorification where a rapid circulation of the blood occurs [105] e.g. blood flow (measured by Doppler) increased by 46% higher in low back pain patients than in controls [106]. Based on that, inflammatory hyperemia brings more blood for clearance during WCT at local inflammatory sites e.g. low back pain and cellulitis to enhance clearance of blood from CPS.

## **9. Al-hijamah for Treatment of Rheumatoid Arthritis (RA) (in Light of Taibah Theory)**

Taking RA as an example, the type of pain is severe in the affected joints which are swollen, tender leading to limited mobility. Treatment options available for RA include analgesics steroids and disease modifying antirheumatoid drugs (DMARD) (potent anti-inflammatory drugs and cytotoxic drugs e.g. methotrexate) [107]. Numerous drug side effects are encountered in pharmacological treatments used for RA e.g. analgesic drugs induce gastritis, gastric ulcers and toxicities at high doses [107], while prolonged steroid therapy causes osteoporosis, hypertension, steroid diabetes, gastric ulcers and steroid dependence [108]. Cytotoxic drugs are strongly harmful at the long term and are the main reason for the intolerable side effects reported in rheumatoid patients e.g. hepatotoxicity, hair fall, exhaustion and fatigue [109]. Unfortunately, despite the big physical, psychological and economic burden of current treatment modalities for RA, resistance to treatment is reported in some cases e.g. many patients with RA experience resistance to a combination of methotrexate and steroids which necessitate searching for better new lines of treatment [110].

In general, treatment modalities are directed towards treating the three Cs (cause, condition and complications). The curative modality of treatment is that treatment that corrects the cause or causes of disease and prevents its pathogenesis. As RA is an immunological disorder characterized by a chronic inflammatory reaction with an autoimmune nature in which auto-antibodies primarily attack synovial joints [83,111] due to increased levels of inflammatory cytokines e.g. tumor necrosis factor (TNF) [111-112], best treatment option is that directed towards correcting the cause. Infliximab (a monoclonal anti-TNF antibody) was reported to be effective in treatment of RA [112]. However, Infliximab is very expensive and carries a lot of side effects. Better results were reported when anti-TNF- $\alpha$  therapy was combined with DMARD therapy in RA patients leading to reduced inflammatory gene expression in whole blood compared to DMARD therapy alone [111]. Reports published in the literature for treating RA using cupping therapy are too few. Cupping therapy for RA was reported to improve pain encountered in those patients. Ahmed et al. reported that cupping

therapy combined with pharmacological treatment for RA dramatically decreased clinical indices of RA as pain severity (measured by visual analogue score), tender joint count, swollen joint count and disease activity scores. Combined cupping and pharmacological therapy also significantly decreased laboratory markers of disease activity as erythrocyte sedimentation rate, C-reactive protein, soluble interleukin-2 receptors (SIL-2R) and rheumatoid factor (RF) which were evaluated over three successive months [5]. Interestingly, while pharmacological treatment for RA-induced leucopenia and decreased count of natural killer (NK) cells (innate immunity), combined cupping therapy and conventional treatment induced leucocytosis with increasing innate immunity (increased levels of NK cells), which was a big advantage in favor of cupping therapy [5]. These immunomodulatory effects of cupping therapy occurred because cupping therapy helped in decreasing the causative immunological reactions underlying the pathogenesis of RA i.e. the decreased level of serum SIL-2R and RF can only be explained through their cutaneous excretion through skin incisions and suction force in cupping therapy which agree with Taibah theory for cupping therapy. This may be a big step towards treating the original cause of that disease. The detailed mechanisms for that were not reported by this research group. Unfortunately, to our knowledge, no similar studies written in English for using cupping therapy for RA were reported. Careful analysis of the reported data may help in understanding how cupping therapy works for treating RA. We propose that cupping technique implied artificial pathways to improve excretion of extracellular tissue fluids, lymph or blood that may be saturated with inflammatory cytokines (as TNF), immune complexes or toxic cellular waste products that are formed in the inflammatory sites. Lack or reduction of those harmful agents through cupping therapy might inhibit the chronic immunological inflammatory reactions or at least decreased their severity or delayed their occurrence. For proper elimination of tissue fluids containing those harmful agents and CPS, suction through creating a negative pressure in the cups may help better drainage of these areas. This is expected to help human body to restore physiological homeostasis according to Taibah theory.

## **10. Al-hijamah for Treatment of Hypertension (in Light of Taibah Theory)**

Obese hypertensive patients were reported to have a higher significant value of extracellular and interstitial fluid volumes than normotensive subjects. At similar blood pressure values, increased extracellular and interstitial fluid volume correlated with the degree of obesity i.e. extracellular and interstitial fluid volumes are increased in obese hypertensive patients and that was related to the degree of overweight and to the mechanisms of hypertension [113]. In some patients with renal hypertension, volume-dependent form of hypertension may occur. Reduction of increased fluid volumes may be essential in the management of these cases [114]. In some studies, renal hypertension was reported to be caused by inhibition of NO synthase (NOS) that synthesizes NO (a vasodilator). This may cause systemic and glomerular hypertension, glomerular ischemia, glomerulosclerosis, tubulointerstitial injury and proteinuria [87,115]. Free radicals e.g. superoxide anions-induced oxidative stress was reported to cause inactivation of NOS and a decrease of the total NO production in human renal hypertension. Oxidative stress occurs early in the course of chronic kidney diseases causing hypertension that increases as the disease progresses [116]. Oxidative stress causes NO deficiency that precedes the development of hypertension [117]. Wang et al. reported severe endothelial dysfunction and inhibition of microvascular NOS in hypertensive patients. That was accompanied by increased levels of plasma ROS and asymmetric dimethyl arginine that can inhibit NOS [118].

In light of Taibah theory, as cupping therapy can drain interstitial fluids and filter excess intravascular fluids full with metabolic noxious substances (CPS) and enhance endogenous NO production, Al-hijamah may be beneficial in treating hypertension. In addition, WCT helps in excretion of accumulated wastes, vasoactive substances and free radicals (causing hypertension) and may be beneficial in treating hypertension.

### 11. Al-hijamah for Treatment of Headache and Migraine (in Light of Taibah Theory)

Cupping therapy was reported to effectively treat headache and migraine, where mean headache severity decreased by 66% following WCT. Treated patients also experienced the equivalent of 12.6 fewer days of headache per month [20]. Recently, serum IL-6 levels were reported to be high in migraine patients both with and without topiramate treatment. This may suggest that high IL-6 levels may play a role in pain attacks in chronic migraine [119]. In light of Taibah theory, migraine and headache can be treated by WCT and this may be due to WCT-induced plasma clearance effect through removal of excess fluids, chemical mediators, IL-6, vasoactive substances, neuropeptides causing headache, decreasing interstitial fluid pressure and treatment of predisposing factors for headache e.g. hypertension [51,113] and acute trigeminal neuralgia [19]. The neuropeptides involved in the pathogenesis of headache include substance P, vasoactive intestinal polypeptide (VIP) and calcitonin gene-related peptide (CGRP) that are important mediators in the pathogenesis of migraine and other primary headaches. Concentrations of CGRP and VIP were reported to be increased in jugular venous plasma during attacks of cluster headache and migraine [120]. Based on that, excretion of the above mentioned CPS may explain how WCT treats headache and migraine.

### 12. Cupping Therapy for Treatment of Cellulitis (in Light of Taibah Theory)

Cellulitis is a bacterial inflammatory reaction in the subcutaneous tissues caused mostly by gram positive bacteria as staphylococcus aureus and streptococcus. Mortality is high in cellulitis due to toxemia and septicemia. Main treatment of cellulitis is broad spectrum antibiotics [121]. Delay in treatment of cellulitis allows for multiplication of microorganisms and production of powerful exotoxins. In case of presence of associated gram negative bacteremia, powerful endotoxins are released causing endotoxic shock [122-123]. This gives the conclusion that antibiotics only may not be enough to treat cellulitis as antibiotics do not affect bacterial toxins. In a recent case report, in a patient with cellulitis, broad spectrum antibiotic treatment was not effective in treatment of that patient. Instead, progressive deterioration in general condition of the patient occurred. Antibiotic therapy together with WCT was done on the site of maximum inflammation of cellulitis by applying about 35 superficial cuts where approximately 9 ml of blood was drawn out. An immediate clinical improvement was noted in the form of reduction in all signs of inflammation. As a good evidence for efficacy of cupping therapy in treating cellulitis, treatment of the same patient for a second time cellulitis using cupping therapy was effective in inducing dramatic improvement [124]. Improvement of cellulitis may be explained in light of Taibah theory where excretion of interstitial fluids and filtered capillary fluids rich in bacteria and bacterial toxins (CPS) helped in clearing blood from microorganisms and toxins and elimination of microorganisms and their toxins outside human body through suction using the negative pressure. Based on that, cupping therapy did better than antibiotics, which did not affect bacterial toxins. Cupping therapy alone allowed removal of both bacteria and toxins

through negative pressure suctioning as evidenced by improvement of patient's condition. The best is to combine both antibiotics and cupping therapy for treating cellulitis.

### 13. Cupping Therapy for Treatment of Fibromyalgia (in Light of Taibah Theory)

Pain due to fibromyalgia is complex and multifactorial in origin i.e. it may be due to interaction of nociceptive, neuropathic, dysregulatory central nervous system factors, metabolic deficiencies in muscle and neurogenic inflammation [125]. Abnormally high cerebrospinal fluid levels of glutamate, substance P, inflammatory cytokines, and ROS are hallmarks of fibromyalgia [126-129]. In fibromyalgia, nociceptive pain is based on the excitation of the nervous sensors by the release of substance P and other neuropeptides from the peripheral nerve endings leading to hyperalgesia due to chemical sensitization at tender points. Neuropathic pain is due to nerve compression as in herniation of vertebral disks or disturbances of axonal transport causing hyperexcitability, disturbed axonal transport system and trophic changes causing tender points in fibromyalgia [125].

Medicinal cupping therapy using dry cupping therapy with drugs in 30 patients with fibromyalgia was reported to be effective in decreasing the severity of fibromyalgia pain and the number of tender points [10,130]. Based on that and on Taibah theory, WCT is expected to be a more suitable and effective treatment for fibromyalgia as it can decrease interstitial fluid pressure, decrease inflammatory cytokines and substance P (CPS via dilution then drainage) and reduce interstitial fluids at sites of inflammation. Evidence for that was the improvement of symptoms of fibromyalgia on using treatments that reduced interstitial fluid at sites of inflammation and the evident anti-inflammatory effects that had been seen [131].

### 14. Cupping Therapy for Treatment of Carpal Tunnel Syndrome (CTS) (in Light of Taibah Theory)

CTS is a common entrapment neuropathy that is predisposed to by many disease conditions e.g. hypertension, RA, diabetes mellitus, hypothyroidism, corticosteroid use, hormonal replacement therapy and wrist fractures [132]. CTS may be drug induced e.g.  $\beta$ -blockers [133]. Pathophysiology of idiopathic CTS was reported to be caused by ischemia-induced reperfusion injury causing an intermittent increase in interstitial pressure, leading to degenerative changes in the flexor tenosynovium and fibrotic changes in the perineural tissue. This may cause alteration in the physical properties of the synovium leading to its rapid and persistent swelling and median nerve compression causing the pain syndrome of CTS [134].

Idiopathic CTS was reported to be an “-osis” not an “-itis” i.e. CTS has non-inflammatory ischemia-reperfusion etiology as evidenced by normal serum interleukin-1 level and elevated serum levels of malondialdehyde. In CTS, tenosynovial levels of malondialdehyde, interleukin 6, and prostaglandin PGE-2 were reported to be elevated compared to controls. Idiopathic CTS causes progressive edema and fibrosis of the tissues within the carpal canal as the source of pain [135].

Metabolic syndrome may cause severe form of CTS three times more common than normal population. Metabolic syndrome includes abdominal obesity, hypertension, dyslipidemia and hyperglycemia [132]. The tissue pressure threshold of normotensive and hypertensive subjects was reported to be consistently 30 mm Hg below diastolic blood pressure which supports the concept that ischemia is the prime mechanism of conduction block in low pressure, nerve-compression CTS [136]. These findings were confirmed later by the study of Husain

et al. who reported that most patients with CTS had dyslipidemia and a large proportion of them had hypertension [137].

In light of Taibah theory, WCT is expected to be a powerful treatment for CTS as WCT can drain tissue fluid containing elevated above-mentioned CPS, decrease pressure of interstitial fluids, resolve synovial swelling, absorb edema fluid and treat predisposing factors e.g. hypertension [51,103], RA [5] and dyslipidemia [45].

### Prophetic Medicine Recommended WCT (Al-hijamah)

Prophetic medicine recommended WCT. Prophetic method of WCT (Al-hijamah) was recently reported to carry better therapeutic benefits than the traditional Chinese method of WCT [138]. Prophet Mohammad (Muhammad) peace be upon him said: "If there is a benefit in any of your treatment modalities, benefit will be in the blade puncture in cupping therapy, a gulp of honey and cauterizing, but I do not like cauterization" [1,139]. Using the expression "in the blade puncture in cupping therapy" means WCT not dry cupping therapy. WCT has an excretory function in clearing blood and tissues from soluble and trapped CPS, while dry cupping therapy has no excretory function. This may give the reason why prophetic method of WCT (Al-Hijamah) was frequently used by prophetic medicine for treating different types of diseases [140]. Using the expression "in the blade puncture in cupping therapy" as a cause of cure summarizes the excretory role of WCT and pays our attention to the fact that cupping therapy opens skin barrier to enhance skin excretory function in agreement with Taibah theory. At this step mentioned in the hadeeth (scarifying skin), negative suction pressure is transmitted from inside cups through skin incisions to create a pressure gradient across skin which causes retained collected fluids in the skin upliftings (mixed with CPS), filtered fluids (containing CPS and harmful materials) and some blood to come out through skin punctures induced by "the blade puncture in cupping therapy". At this step mentioned in the hadeeth (puncturing skin), negative suction pressure is transmitted from inside cups through skin incisions to reach around capillaries to create a pressure gradient across capillaries to filter capillary fluids filled with soluble mediators and CPS. The prophetic term "blade puncture, shartatmihjam in Arabic language" is so precise medically and scientifically. Blade puncture means scarifications of skin (longitudinal very superficial incisions about 0.1 mm in depth) not just pin-point pricks, which confirms the target of Al-hijamah that is inducing openings in skin barrier enough to excrete CPS (in agreement with Taibah theory). It can be concluded from these prophetic sayings that WCT is not a mere bleeding or venesection. If cupping therapy aims at only getting rid of blood, it is easier to injure a superficial vein to start bleeding with no need for negative pressure application.

Moreover, best therapeutic outcomes occur on combining current pharmacological treatment modalities with WCT. Taking RA as an example, conventional treatment modalities aim to suppress inflammatory reactions, while WCT powerfully withdraws CPS e.g. SIL2-R to outside the body (as evidenced by its decreased level in venous blood after WCT) which will result in suppression of inflammatory reactions in RA [5]. Excretory role of WCT may be a very potent treatment to many diseases in which harmful substances cannot be excreted outside human body.

However, practicing cupping therapy using pressure suction force, minimal skin scarifications (about 0.1 mm in depth to open skin barrier, horny layer of epidermis) and pressure suction force for the second time at skin sites away from superficial veins confirms that WCT is an excretory rather than a mere bleeding procedure. Removing noxious agents to outside human body seems more safe and effective than

antagonizing or relieving their harmful effects using pharmacological drugs. In prophetic medicine, the method for creating negative pressure suction in WCT was the manual suction [141], which is reported now to exert a suitable reproducible pressure [37].

Honey is another curative remedy in prophetic medicine [1,139]. Applying honey before Al-hijamah is beneficial to fix sucking cups at skin points. Applying honey locally to skin scarifications after Al-hijamah helps rapid healing. In a German report, wound healing using honey was achieved in patients whose wounds were either infected or colonised with methicillin-resistant *Staphylococcus aureus*. Antiseptics and antibiotics had previously failed to eradicate the infection [142].

### Conclusion and Recommendations

Al-hijamah is a minor surgical excretory procedure that has medical and scientific bases in clearing blood and interstitial spaces from harmful substances, noxious substances and CPS. Both modern medicine and prophetic medicine proved the beneficial value of WCT in treatment of diseases that are different in etiology and pathogenesis. The Chinese are pioneering in practicing cupping therapy in their hospitals. We recommend practicing Al-hijamah officially in hospitals for treating human diseases for the great benefits of this promising line of treatment. WHO is invited to shed more light upon health benefits of Al-hijamah and to encourage its practice in hospitals. Ministries of health worldwide and in the motherland of the prophetic medicine (Saudi Arabia) are invited to allow and encourage the practice of Al-hijamah in hospitals officially in a pure medical atmosphere close the way in face of unqualified malpractitioners. Ministries of health worldwide and in the homeland of prophetic medicine (Saudi Arabia) are invited to allow and encourage the practice of Al-hijamah officially in hospitals to benefit patients, relieve pain and to decrease human suffering.

Miraculous remedies in prophetic medicine are a heritage (legacy) for the whole humanity. The prophet peace be upon him is being described as a mercy for all people [143]. Researchers worldwide are invited to pay more attention to develop more research in investigating remedies practiced in prophetic medicine to cure and relieve human suffering in many incurable diseases with dismal prognosis. Such remedies include Al-hijamah, Al-kost Al-bahri, Al-kost Al-Hindi (*Costusspeciosus* SM), miswak (*Salvadorapersica*), honey, Happah sawdaa (*nigella sativa*), olive oil, kamaa (*Terfeziaceae*, desert truffles), vinegar, sana, sanut, Zamzam water, dates of Madinah (ajwah of Aliah) and others.

The majestic deep-rooted Egyptian Universities as Al-Azhar, Cairo, Alexandria Universities and the internationally ranked King Saud University, Taibah University, Islamic University in Al-Madinah and Om Al-Quraa University in Makkah in Saudi Arabia (homeland of prophethood) are invited to guide research to introduce remedies in prophetic medicine to scientific and medical humanity literature. The pioneering report of Sahbaa Ahmed (Al-Azhar University) in treating RA with Al-hijamah [5] is well cited and appreciated.

### Acknowledgements

We are so grateful to the library of Sohag faculty of medicine, Sohag University, Egypt for providing the internet facility and helpful textbooks.

The authors declare that there is no conflict of interest.

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