

Diabetes prevention and treatment with Greco-Arab And Islamic-based natural products

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Abstract

Diabetes has been recognized by medieval Greco-Arab physicians and its main symptoms were known by the increased thirst, frequent urination, and tiredness. Arab and Muslim physicians had used series of medicinal plants for treating these combined symptoms (named Zarab). In addition to several instructions for specific food consumption, a mild exercise was recommended. Currently, traditional Arab-Islamic medicine continues to be practiced in most Arab and Islamic countries. The current form of Arab and Islamic herbal medicine has historical roots in medieval Greco-Arab and Islamic medicine. This medicine has influenced Europe where it formed the roots from which modern Western medicine arose in late middle ages and early European medical education. It is important to highlight that the Greco-Arab and Islamic medicine was not a simply translations and continuation for Greek ideas but rather a venue for innovation and change. This review article provides a comprehensive overview on traditional Arab-Islamic herbal medicine including the historical background, medical innovations introduced by Arab physicians, methods of therapies, and a state of the art description of traditional Arab herbal medicine.

KEYWORDS: Arab-Islamic herbal medicine; diabetes type II, Avicenna, Rhazes.

INTRODUCTION

Currently, we are witnessing a great progress in evidence-based modern medicine and pharmacology. The characterization of pharmacological and biological effects of herbal-based medicines is becoming more competitive and complex, with the involvement in this research area of experts belonging to different scientific fields, including botany, chemistry, biochemistry, immunology,

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molecular biology, and bioinformatics. However, despite this great progress in evidence-based modern medicine and pharmacology, traditional Arab-Islamic medicine continues to be practiced within the Mediterranean as well as most Arab and Islamic countries. The current form of Arab and Islamic herbal medicines use has historical roots in Greco-Arab and Islamic medicine, which was flourished in the golden age (seventh to fifteenth century) of the Islamic civilization. The Arab and Muslim world refers in geopolitical sense to Muslim majority countries or countries in which Islam dominates politically. Arab-Islamic community is spread across many different nations and ethnic groups connected only by religion. Medicine and pharmacology in general are considered to be one of the most illustrious and best known facets of Arab-Islamic civilization in which Arabs most excelled. In the history of medicine, Islamic medicine, Arabic medicine, or Greco-Arab and Islamic medicine refers to medicine developed in the golden age of the Islamic civilization and written in Arabic, the lingua franca of the Islamic civilization [1-4].

Ancient Greek physicians like Hippocrates (460 – 370 BC) laid the foundations of the Arab-Islamic and modern theories (Figure 1). Hippocrates proposed that thoughts, ideas and feelings, originate in the brain, can influence health and the process of disease. Arab and Muslim physicians proposed that the body should be treated as a whole and not just as a series of tissues and organs, and that it was endowed with an ability of natural healing, which depended on rest, a good diet, fresh air and cleanliness. Rhazes (846-930) supported this concept by his recommendation: *"The physician, even though he has his doubts, must always make the patient believe that he will recover, for state of the body is linked to the state of the mind."* Later on, Ibn Sina (980-1037) who defined medicine as *"the science from which we learn the states of the human body with respect to what is healthy and what is not; in order to preserve good health when it exists and restore it when it is lacking"* supported the views of Rhazes. He stated that *"We have to*

understand that the best and most effective remedy for the treatment of patients should be through the improvement of the power of the human body in order to increase its immune system, which is based on the beauty of the surroundings and letting him listen to the best music and allowing his best friends to be with him".

It is now clear that the mind and the body interact, influence and regulate each other. Recent research has indicated that the perception of stress can lead to production of 'stress hormones', as well as cytokines produced by cell of the immune system. These 'stress hormones' act in a feedback mechanism to regulate their own production and the production of certain cytokines. These cytokines act on the brain to modify behavior and the ability to perceive and to respond to stressful challenges by inducing lethargy, fever and nausea (i.e. 'sickness behavior').

Based on recommendations of Rhazes and Avicenna, Greco-Arab and Islamic healers treated patients through a scheme starting with physiotherapy and diet; if this failed, drugs were used. Rhazes's treatment scheme started with diet therapy, he noted that "*if the physician is able to treat with foodstuffs, not medication, then he has succeeded. If, however, he must use medications, then it should be simple remedies and not compound ones*". Drugs were divided into two groups, simple and compound drugs. Physicians were aware of the interaction between drugs, thus, they used simple drugs first. If these failed, compound drugs, consisting of two or more compounds were used. If these conservative measures failed, surgery was undertaken [1-8].

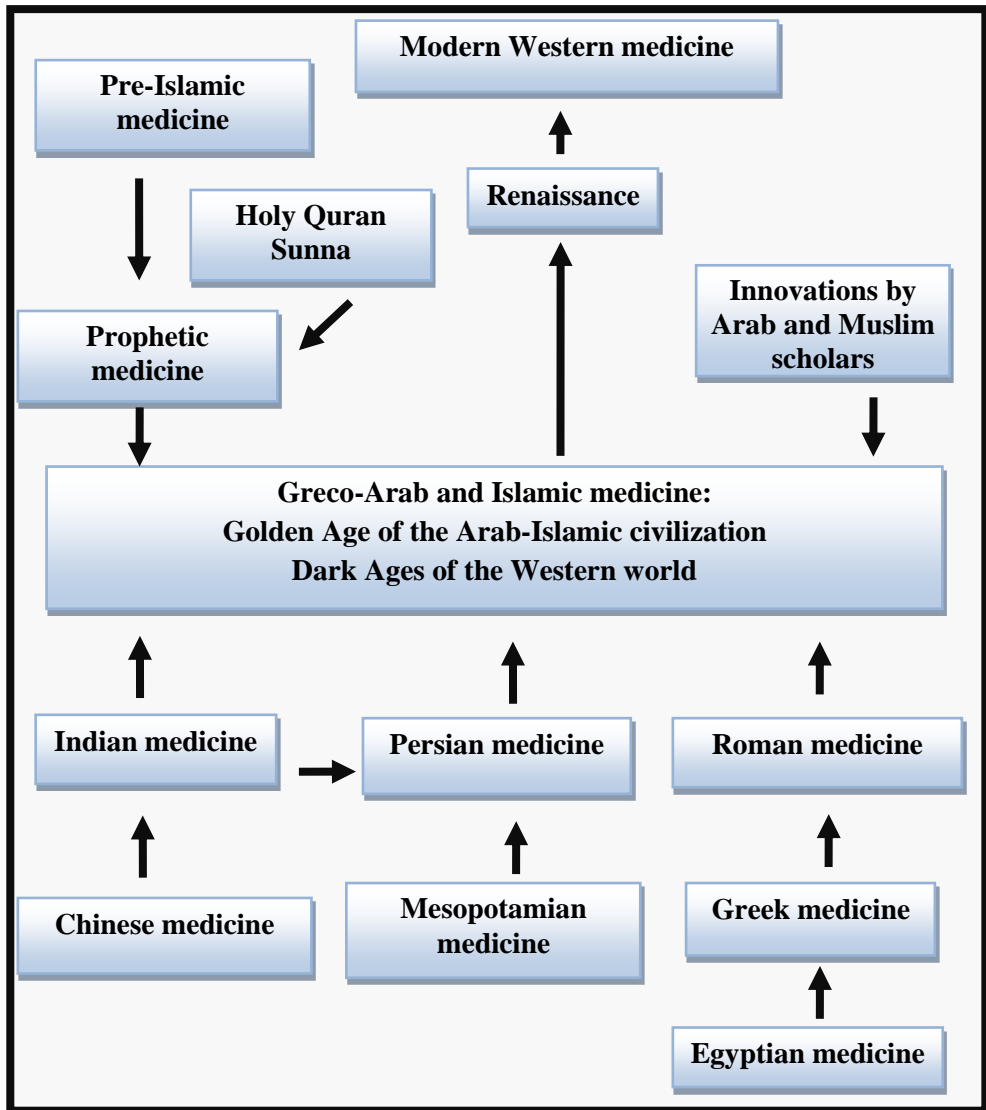


Figure 1. Development of Greco-Arab and Islamic medicine.

Greco-Arab medicine history at a glance

The Greco-Arab and Islamic medicine is divided into three phases: Phase I, Greek into Arab; Phase II, Arab; and Phase III, Arab into Latin. The first phase of the Greco-Arab and Islamic medicine was the period of translation of Greek scientific and philosophical works into Arabic. This started in the eighth century when Islam covered nearly two-thirds of the world (known at their time). The Khalifa al-Ma'mun established 'The House of Wisdom' in order to translate the Greek science. Large number of medical works of Hippocrates and Galen, as well as philosophical works by Plato and Aristotle and mathematical works of Euclid and Archimedes were translated into Arabic. Hospitals and medical schools flourished during that period, first in Baghdad and later in the main provincial cities.

The second phase began when the chief works of Galen and Hippocrates were made available in Arabic, Christians lost their monopoly of medicine, and several Muslims reached such a stature in medical science that they stood far above their immediate predecessors and were roughly on a level with the greatest of the Greeks. Some notable scholars of the science of Arab medicine were: *Al Tabbari* (838-870), *Al Razi* (Rhazes) (846-930), *Al Zahrawi* (930-1013), *Ibn Sina* (Avicenna) (980-1037), *Ibn Al Haitham* (960-1040), *Ibn Al Nafees* (1213-1288), and *Ibn Khaldun* (1332-1395).

The third phase "Arab into Latin" began in the twelfth century when European scholars who were interested in science and philosophy came to appreciate how much they needed to learn from the Arabs. As such, they set about studying Arab manuscripts in these disciplines and translating the most important ones into Latin. The most outstanding writer on medicine in Arabic was Ibn Sina, or as he was known in the West, Avicenna. Like Al Razi, Ibn-Sina wrote on many subjects, and was known to have been a greater philosopher than a physician. Nevertheless, his

vast "Canon of Medicine" is rightly acclaimed as the "culmination and masterpiece of Arab systematization." It was translated into Latin in the twelfth century, and continued to dominate the teaching of medicine in Europe until at least the end of the sixteenth century. There were sixteen editions of Ibn Sina's work in the fifteenth century, twenty editions in the sixteenth century, and several more in the seventeenth century. His book classifies and describes diseases, and outlines their assumed causes. It also discusses hygiene, simple and complex medicines, the symptoms and complications of diabetes, and functions of parts of the body. Ibn Sina even asserted that tuberculosis was contagious, which was later disputed by Europeans, but turned out to be true [1-6].

Innovations introduced by Arab physicians

Avicenna was the first to use ice to treat fever diseases and separate medicine from pharmacological science. Arab physicians introduced the use of animal testing and combined different sciences such as chemistry, medicine, pharmacology, agriculture, and plant science in order to develop new treatments for their patients. In surgery, Al Zahrawi was the first to develop various surgical equipments and tools, some of which were unique for surgery on females. Later on, Ibn Al Haitham improved the surgery of eyes and studied the process of sight for the first time. Arab doctors were also aware of the contagious qualities of diseases. Other medical innovations introduced by Arab and Muslim physicians included: The discovering of the immune system and the introduction of microbiological science. [1-6].

Arab physicians introduced many new ideas and upgraded the knowledge about herbs and their potential medical efficacy and safety. For example, Al-Rhazes discovered the origin of smallpox and showed that one could only acquire it once; indicating the existence of the immune system. Jaber Ibn Hayan and others extracted different anesthetic compounds from local herbs for local or general

anesthetization. Daoud Al-Antaki, used different herbs for treating patients and published a book on medicinal herbs summarizing the knowledge of his predecessors. Ibn Al-Bitar, in Andalusia, Spain, introduced around 350 new plant species as medicinal herbs for treating human diseases. Abu Al-Abbas and other herbalists published several books and dictionaries on the use of medicinal plants describing each plant species, the plant parts used, the preparation procedure used for each remedy, and the treatment procedure of certain diseases. Avicenna published several books such as "Alkanoon Fi Altib" (Canon of Medicine) in addition to Rhazes book "AlHawy" (The comprehensive), which were translated into several different languages. Up until a few centuries ago, these two books were the primary medicinal literature, and they are still in use in different libraries in Europe [7-13].

At the Eighth-century, Arabs in Baghdad region were the first to separate medicine from pharmacological science (Figure 2). At that point, patients started to deal with experts in the pharmaceutical sciences working on the extraction and preparation of remedies, and not with physicians who were now responsible for the diagnosis of diseases and follow-up with the applied treatments. This fact resulted in a huge development in pharmaceutical science; pharmacologists and ethno pharmacologists started to search for different ingredients and extracts to be used as remedies, and they even started to study the chemical properties of the materials used in the treatment of various diseases and ailments. For the first time, chemists such as Jaber Bin Hayan started to search for methods to extract and purify different compounds including alcohol, nitric acids, sulfuric acids, and royal acid. The latter was used to dissolve gold. Abu Bakr Al-Razi (Rhazes) was the first to use animal gut for suture material. He had also started to use animals in the laboratory in order to test the safety and efficacy of the extracted active ingredients. The first animal used in these experiments to test the effects of mercury on the body was a monkey [7-13].

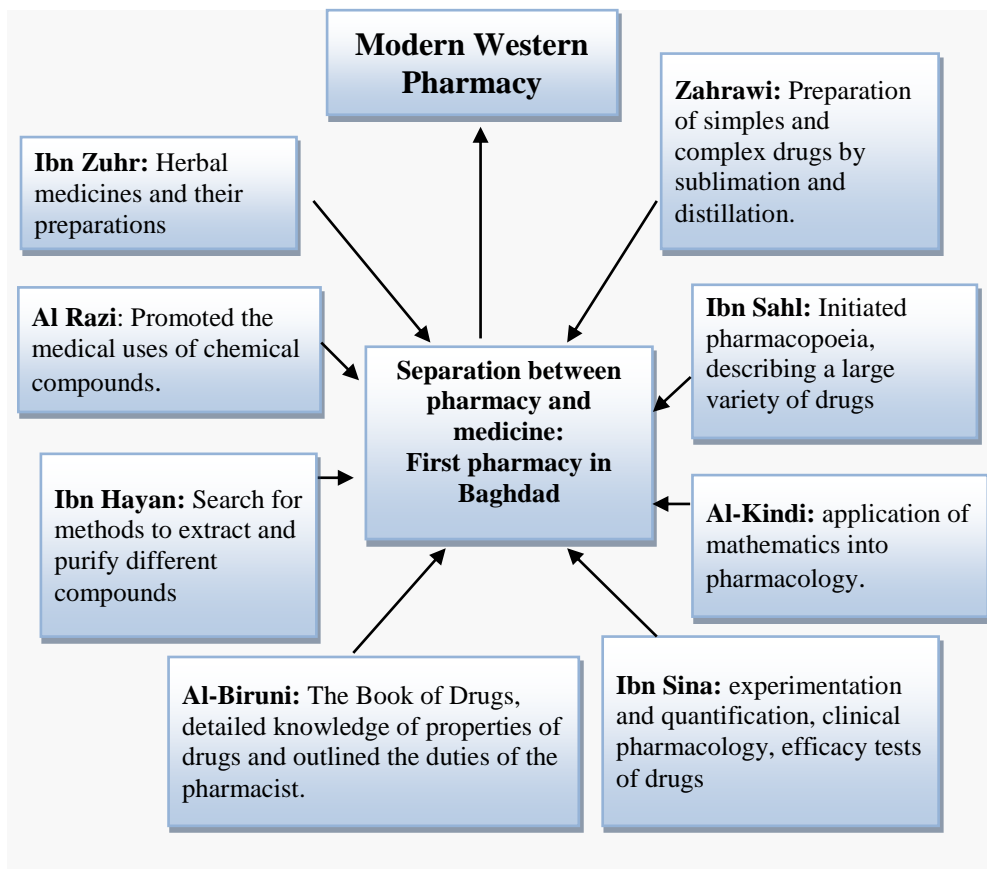


Figure 2. Development of Arab-Islamic and modern pharmacy.

Chemists such as Jaber Bin Hayan started to search for methods to extract and purify different compounds. Avicenna devoted a whole volume to simple drugs in Canon. He described about 700 preparations, their properties, mode of action and their indications. Rhazes promoted the medical uses of chemical compounds. Al-Zahrawi (Abulcasis) described a large number of recipes and explained how to prepare the simple drugs as well as complex drugs. Shapur ibn Sahl, was, however, the first physician to initiate pharmacopoeia, describing a large variety of drugs and remedies for ailments. Al-Biruni gave in his Saydanah fit-Tib detailed knowledge of the properties of drugs and outlined the role of pharmacy and the functions and

duties of the pharmacist. Al-Kindi introduced the application of mathematics into medicine, particularly in the field of pharmacology.

Diabetes in Greco-Arab medicine

Herbal-based anti-diabetic medicines have been a part of traditional medicine for centuries. Plants have been used for medicinal purposes for as long as history has been recorded. Mesopotamia, Egypt, China, India, and later on the Arab Islamic world appear to have been the places which cradled the use of herbs. In addition to plants, other natural products from animals and minerals have also been used as a source of medicines from ancient times. Hundreds of wild plants as well as wild and domestic animals and their by-products (e.g., bones, feathers, hooves, skins, and tusks) form important ingredients in the preparation of curative, protective and preventive medicine.

The Chinese were the first who detected diabetes (in the third century), they noticed that the sweetness of urine attracts dogs. Later on, Indian physicians (in the sixth century) related to diabetes as "Honey urine" and prescribed several herbs to treat it [14]. Diabetes was recognized by medieval Greco-Arab physicians by its main symptoms: increased thirst, frequent urination, and tiredness. Greco-Arab physicians and practitioners had used series of medicinal plants for treating these combined symptoms (named Zarab). During the ninth and tenth centuries, Rhazes (846–930), translated and enriched the Arabic literature with information about diabetes. The basic source which he relied upon was the Hindu writings beside his valuable contribution [15]. Rhazes said: "*I use in the treatment of diabetes things that cool thirst and thickens the blood*". He recommended sitting in water until the skin turns green because it tightens the bladder muscle, cools the kidney and stops thirst and perscribed licorice [10].

Avicenna described diabetes as: "*diabetes is that the water exits [from the body] as it was drunk, in a short time*" [9]. According to Avicenna, diabetes is caused by

malfunction of the kidneys, namely weakness or an excessive attraction of moisture. The kidney naturally has to push the surplus moisture forward, since it attracts much more moisture than it can maximally retain. Avicenna prescribed emetics and medicines that stimulate perspiration for diabetes. He recommended avoiding foods that stimulate urination and to exercises [16].

Treatment of type 2 diabetes revolves around controlling circulating glucose levels (either through glucose production or utilizing or through increasing insulin secretion and effectiveness) or by reduction of energy intake or increasing energy expenditure. The natural herbs for diabetes treatment focus on lowering blood sugar and reducing the damaging effects of the disease. The anti-diabetic mechanism of plant are usually: insulin sensitizer, insulin mimics, insulin secretagogues and inhibitors of intestinal carbohydrate digestion and absorption.

Insulin sensitizers include plants that increase glucose uptake and disposal by muscle, fat and hepatic cells as well as those that regulate hepatic glycogen metabolism. In this category, garlic (*Allium sativum*) and onion (*Allium cepa*) decrease blood glucose levels by normalizing liver hexokinase and glucose-6-phosphatase activity [17]. *Nigella sativa* and *Cinnamomon cassia* (cinnamon) were suggested to have insulin mimetic properties, through enhancing insulin signaling pathway independently of insulin [18]. The comonly used Greco-Arab anti-diabetic herbs are summerized in table 1.

Table1. Medicinal Plants Used to Treat Diabetes Based on the Traditional Arab Medicine

Latin name	Arabic name	Part used
<i>Achillea fragrantissima</i>	Kaisom قيصوم	leaf and stem
<i>Achillea millefolium</i>	Akhilia em alf waraka إخيليا أم ألف ورقة	leaf and flower
<i>Allium cepa</i>	Basal بصل	bulb and seed
<i>Artemisia Arborescens</i>	Sheba شيبية	leaf
<i>Artemisia herba-alba</i>	Sheh شيع	foliage
<i>Asparagus aphyllus</i>	Halion هليون	shoots
<i>Atriplex halimus</i>	Qataf قطف	leaves
<i>Bidens pilosa</i>	Huseke حوسيكه	whole plant
<i>Centaurea iberica</i>	Murrar مرار	whole plant
<i>Ceratonia siliqua</i>	Kharob خروب	leaves, fruits and seeds
<i>Cichorium pumilum</i>	A'elet علت (هندباء)	leaves
<i>Citrullus colocynthis</i>	Hanzal حنظل	seeds, fruits and fruit pulps
<i>Coridothymus capitatus</i>	Zaa'tar faresi زعترا فارسي	foliage
<i>Crataegus aronia</i>	Zaa'ror sha'ek زعرور شائك	fruit, flower and leaves
<i>Cupressus sempervirens</i>	Saro سرو	fruit and leaf
<i>Inula viscosa</i>	Tayyon طيون	foliage
<i>Juglans regia</i>	Juz جوز	leaf and flower

Latin name	Arabic name	Part used
Lupinus albus / pilosus	Tormus barre ترمس بري	seed
Lycium europaeum	A'awsaj عوسج	root
Mercurialis annua	A'eshbet el jarat عشبة الجارات	leaf
Morus nigra	Tot توت	leaf, stem and fruit.
Olea europaea	Zaiton زيتون	leaf and fruits
Paronychia argentea	Rejel El hamama رجل الحمامة	leaf and flower
Pinus halepensis	Snobar صنوبر	leaf and seed
Portulaca oleracea	Farfahena فرفحينة	foliage
Quercus calliprinos	Ballot بلوط	fruit and bark.
Salvia fruticosa	Merameye مريمية	foliage
Sarcopoterium spinosum	Bellan بلان	leaf, seed and root
Teucrium capitatum /polium	Jea'det el sebyan جعدة الصبيان	foliage
Trigonella foenum- graeceum	Helbe حلبة	seed
Urtica dioica	Qurres قريص	Foliagle and seeds

Traditional herbs as a novel source for anti-diabetes treatment

To consider anti-diabetic plants for clinical use, the ideal plant has to possess the following properties: has traditionally been used in more than one country, has experimentally documented constituents, hypoglycaemic activity and very low toxicity as well as to be botanically abundant. According to recent surveys carried

out among practitioners of Arabic medicine in the Middle East, 26 plant species for the treatment of diabetes mellitus have been disclosed. We had tested four of the best anti-diabetic herbs candidates: *Juglans regia* (walnut), *Atriplex halimus* (saltbush), *Olea europaea* (olive), and *Urtica dioica* (nettle). A mixture of these four antidiabetic herbs was developed according to the extensive herbal knowledge of the Greco–Arab medical system [19]. The safety and efficacy of this mixture (Glucolevel) were tested in our laboratories. We hypothesized that extracts from the four plants when combined may disclose synergistic effects on different levels of glucose-insulin homeostasis adding thus to the therapeutic efficacy.

Following the evaluation of Glucolevel anti-diabetic activity in animal models, sixteen test persons were recruited for our study. Their ages ranged from 48 to 67 years and none of them took any pharmacological drug during the study period (four weeks). They were asked to continue their daily activities and diet habits unchanged and to take one tablet of Glucolevel three times daily. They were also asked to restrain from consuming any medications during the study period. Each subject was given a free-of-charge box containing 90 tablets of Glucolevel and was asked to fill an informed consent.

No minor or major adverse effect was noted and the Glucolevel was well tolerated by all subjects. During the first week of Glucolevel consumption, baseline glucose levels were reduced from 290 ± 40 to 210 ± 20 mg/dL in these subjects. According to baseline glucose levels, a subgroup of 11 subjects had glucose levels below 300 mg/dL and the other subgroup had levels above 300 mg/dL. The former subgroup achieved clinically acceptable glucose levels during the second and third weeks of Glucolevel consumption. The higher blood glucose level subgroup, needed one week more to achieve clinically acceptable glucose levels.

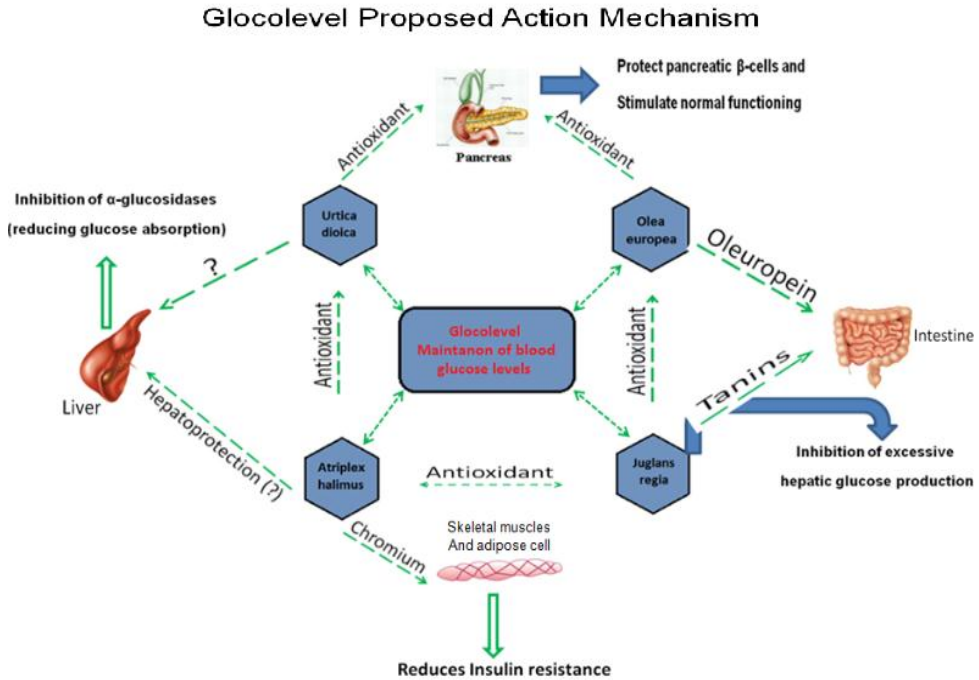


Figure 3: Proposed Glucoselevel mechanism of action.

Glucoselevel proposed action mechanism. Scientific evidences obtained so far indicate hypoglycemic and antioxidant properties of each of the four herbs contained in Glucoselevel.

a) Olive leaf extracts possesses antibiotic, anti-aging, immunostimulator as well as anti-diabetic properties. In clinical studies, Olive leaf lowered blood and act as antibacterial, antifungal, and anti-inflammatory agent in vitro [20]. The main active ingredient in olive leaf is oleuropeoside that disclosed a distinct hypoglycemic effect at a dose of 16 mg/kg, concomitant with hypotensive and hypolipidemic properties. Oleuropein aglycone is also believed to be effective against type 2 diabetes because of its protection against aggregate cytotoxicity reported using a RIN-5F rat insulinoma cell model. Antioxidant effect of olive oil in pancreatic β cell has been documented. Oleic acid has been shown to increase

insulin production and to reverse the inhibitory insulin effect of tumor necrosis factor alpha (TNF- α) in the rat pancreatic beta cell line INS-1. In islets of Langerhans from mice supplemented with extra virgin olive oil, the expression and activity of the antioxidant enzymes, catalase and glutathione peroxidase, were increased significantly. Furthermore, after incubation with hydrogen peroxide, islets from extra virgin olive oil-supplemented mice had a higher glucose-stimulated insulin secretion compared to the control group. *In vitro* investigations have found that olive oil phenols are potent antioxidants, which may provide potential chemoprotective properties [20].

b) Tannins and polyphenolics in walnut leaves were found to be potent antioxidants and reveal a strong scavenging activity against both superoxide and hydroxyl radicals [21].

c) Saltbush is an extremely effective antidiabetic herb and shows an insulin potentiating effect in animal model for diabetogenesis and obesity [22]. *In vitro* experiments have shown that Glucosyl facilitates glucose entry into yeast cells during anaerobic fermentation. This observation may be attributed to an effect of saltbush content on Glucosyl.

d) *Urtica dioica* extracts can be used to treat arthritis, hay fever, kidney problems, pain and anemia. Moreover, its extract is in use to stop bleeding because of its high Vitamin K content and was shown to reduce TNF- α and other inflammatory cytokines [23]. The nettle extract is effective in lowering blood glucose levels via decreasing glucose production by the liver. Such an effect was evidenced in our experiments with the inverted intestine segment.

Conclusions

Greco-Arab herbs have been used for hundreds of years either in their crude forms or as herbal teas, syrups, and powders in treatment and prevention of diverse diseases including diabetes [24-29]. Despite the mentioned remarkable successes in all aspects of medicine, Greco- Arabic medicine did not provide strong achievements in the treatment of diabetes due to inability to understand and diagnose correctly the diabetes, besides the complete relaying on the four humor theory in the drug discovery process.

The four humor theory is believed to be a serious knowledge barrier for the classic medical Greco-Arabic medical system and prevented understanding and diagnosing diabetes correctly. Nevertheless, the non-philosophic Arabic traditional medicine was free to offer us a long list of effective herbs for treating diabetes. More than 50% of the modern pharmaceuticals used in conventional medicine today have natural plant origins. Among them the anti-diabetic drug, metformin, was derived from the flowering plant, *Galega officinalis* (Goat's Rue or French Lilac), which was a common traditional remedy for diabetes [30].

Nowadays, alternative herbal-based treatments for diabetes mellitus is prevalent in most Arab and Islamic countries, these medications are unregulated and are not standardized which poses a risk for their use, although some would debate that natural ingredients would not be harmful to their health unless taken in significantly increasing amounts. Any medication, be it herbal or chemical, should always be taken in moderation. We believe that it's the researchers and physicians responsibility to provide scientific evidence based of traditional health care and promote health literacy for diabetic subjects.

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تلخيص:

تم اكتشاف مرض السكري من قبل أطباء عرب ويونان في العصور الوسطى وكانت أعراضه الرئيسية تعرف من زيادة العطش وكثرة التبول والإرهاق. وكان الأطباء العرب والمسلمون يستخدمون تشكيلة من النباتات الطبية لمعالجة تلك الأعراض مجتمعه وتسمى (زراب). هذا بالإضافة إلى تعليمات متعددة لاستهلاك أغذية محددة، والنصح بتأدية تمارين رياضية خفيفة. لا يزال الطب التقليدي العربي الإسلامي يستخدم حالياً في معظم الأقطار العربية والإسلامية، علماً بأن طب الأعشاب العربي الإسلامي بشكله الحالي تمتد جذوره التاريخية إلى الطب العربي الإسلامي في العصور الوسطى. هذا الطب كان له تأثيره على أوروبا حيث تشكلت منه الجذور التي انبثق منها الطب الغربي الحديث لاحقاً في نهاية العصور الوسطى والتعليم الطبي الأوروبي المبكر. ومن المهم التنويه إلى أن الطب العربي والإسلامي - الإغريقي ليس مجرد ترجمة أو استمرار للأفكار الإغريقية بقدر ما هو صرح للابتكار والتغيير. ويهدف هذا المقال إلى إلقاء نظرة عامة وشاملة على طب الأعشاب العربي الإسلامي التقليدي بما في ذلك خلفيته التاريخية والابتكارات الطبية التي ادخلها الأطباء العرب بالإضافة إلى طرق العلاج والوصف الفني الذي قدمه طب الأعشاب العربي التقليدي.