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Avicenna (980-1032CE): The Pioneer in Treatment of Depression

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Abstract

Background: The aim of this study is to clarify Avicenna's point of views on neurology and psychiatry especially depression. Avicenna who is known as prince of physicians had a great contribution on medicine. He was a scholar not only in medicine, but also in logic, philosophy, astronomy and mathematics. Second volume of his masterpiece in medicine, "The Canon of Medicine", has a chapter on neurological and psychiatric disorders. The book is divided into 5 volumes which was one of the main medical references in the east and the west until 17th century CE. Avicenna has considered different aspects of sadness and depression and pointed out to the relation between depression and various diseases.

Materials and methods: The Canon of Medicine as the most important reference of traditional Persian medicine has been searched on keywords such as "melancholia" and "sadness" to find the most overlap with the definition of depression. The extracted texts were finally compared with modern medicine.

Results: According to the traditional Persian medicine, mental states have direct effects on human well-being and development of diseases. Avicenna prevented and managed depression based on lifestyle modification, natural remedies and manipulation. Happiness, aromatherapy, and music therapy are common treatments for most diseases.

Conclusion: About 30 medicinal herbs have been introduced by Avicenna for treating and managing depression. Some of which have been emphasized to have antidepressant effects via clinical trials. A scientific review of Avicenna's other proposed methods and terms can result in new treatments for depression.

Keywords: Avicenna, depression, melancholia, Persian medicine

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"for long the rule held that he who would be a good doctor must be a good avicennist." manfred ullmann (1940-90 CE)

Introduction

Depression has become so common that is categorized as the second chronic disorder after hypertension in general medical practice Whooley & Simon. (2000). Despite the existence of efficient treatments for depression, more than 50% of patients do not gain significant clinical rescue. Treatment resistance is most likely to happen along with physical and mental disorders with the presence of extended and marked functional deterioration simultaneously with functional weakening Wehbe *et al.* (2014). On the other hand, clinical evaluation of modern antidepressants has shown incidence of side effects and drug interactions. Due to these problems, presentation of new sources for finding antidepressants like natural products is essential Rajput *et al.* (2014).

Nowadays, patients in developed and developing countries choose traditional medicine as solitary or complementary therapeutic choices Abolhassani *et al.* (2012). Scientific reassessments of old medical sources can be a futuristic approach for discovering new answers for old questions. Persian medicine (PM) is one of the firstborn schools of medicine in the history Zargaran *et al.* (2013).

PM dates back to about 10000 years ago in ancient era. Later, medieval Persian practitioners (during 8 -12th century CE) were conversant with the medical theories of ancient Persia, Greece, Egypt, India, and China. The Persians not only collected whole available medicine in that time, but also added their own precise experimentations and interpretations to this knowledge

and presented numerous new scientific concepts Gorji & Ghadiri. (2002), Naseri & Namavar. (2014).

In Persian Medicine (PM), alike considered in Chinese Medicine (CM), the human body classified into some temperaments based on signs and symptoms, but with different protocols Rezadoost *et al.* (2016).

The Structure of Persian Medicine is based on two main divisions, theoretical branch which describes situation and changes of the human body and a practical division which is the skill of how to maintain health and how to restore it after the outbreak of the diseases Rezaeizadeh *et al.* (2009). Some of Persian physicians in that time may be known as the pioneer psychiatrists and psychologists, even before considering of psychology as a distinct field of science. They qualified stringent and explicit clinical manifestation of various psychological disorders. They established the first psychiatric hospitals and separate wards in general hospitals Najmabadi. (1996). Among the Persian physicians in the early medieval era (9-12th century CE) which is called as Islamic Golden Ages, Avicenna was a Persian physician who had effulgence contribution in medical sciences, in particular in the field of neuroscience and psychiatry regarding its effects on philosophic thoughts Vakili & Gorji. (2006).

Abu Ali Husain Ibn Sina who is known as Avicenna (Figure 1) in the west, was born on 23 August 980 CE in the ancient Persian city of Afshaneh, near *Bukhara* Zargaran *et al.* (2012). He was a talented child and by the age of 10 he would become well versed in science and logic. At the age of 18, he became a famous physician Golzari *et al.* (2013).



Figure 1: Portrait of Avicenna (980–1037 CE). Depicted by Saber Baggal Asghari and Babak Kamal Gazani (with permission).

Avicenna expressed his interest in medicine as follow: "Then I desired to study medicine, and took to reading the books written on this subject. Medicine is not one of the difficult sciences, so naturally I became proficient in it in the short time, until the excellent scholars of medicine began to study under me. I began to treat patients, and through my experience I acquired an amazing practical knowledge and ability in methods of treatment." Modanlou. (2008).

Three characteristics which distinguished Avicenna from his contemporaries were permanence in learning, thoroughness and wonderful memory. They were definitely relevant to his great successes at such a young age Erolin *et al.* (2013). Avicenna's glory and influence was not only appreciated in Iran and the Islamic countries, but also was a famous scholar in the world. He is still known as an ecumenical scientist particularly in medicine to physicians and historians Moosavi. (2009).

Although there is an argument concerning the number of books endorsed to Avicenna, he wrote at least 276 treatises. His masterpiece in the doctrine of medicine is "Al- Qanun fi al-Tibb" (Canon of Medicine) which was a significant educational resource in European universities between 13th and 17th centuries Shoja *et al.* (2009). Latin translations of Avicenna's book were issued consecutively 16 times and more than 20 times in the last three decades of the 15th and 16th centuries respectively and it continued to be printed

and widely read until the seventeenth century Afnan. (2015).

The book is divided into 5 volumes, in which psychiatry and brain disorders are described in the third volume. A variety of illnesses are discussed in *Canon of Medicine* covering all parts of the body, from head to toe, and each illness is described in terms of its pathology, signs, prevention and therapy Ibn Sina. (1997). For example, the love disorder explained by him as an obsessive disorder looks like a severe form of depression in which the patients are suffering from an excess of imaginary figures and obsessive ideas. Actually, the disease is categorized by poor grooming, dry and hollowed eyes Shoja & Tubbs. (2007). particularly, he has described concepts such as mind, soul, wisdom, man's desire, and dream. He discovered that some physical diseases were produced by emotional upsets Namazi. (2004).

In another book by Avicenna entitled "Kitab al-Adviyt-ol-Qalbiye" (book on drugs for cardiovascular disease) (Figure 2), drugs associated with psychiatric and cardiovascular diseases are mentioned (Ibn Sina, 2009). Translations of the book were available in Latin under the title of "Medicamenta Cordialia", in Turkish and Urdu Tekol (2007). Although some articles have mentioned to the important role of this book in the field of cardiology, but the significant effect of exhilarating drugs in treatment of

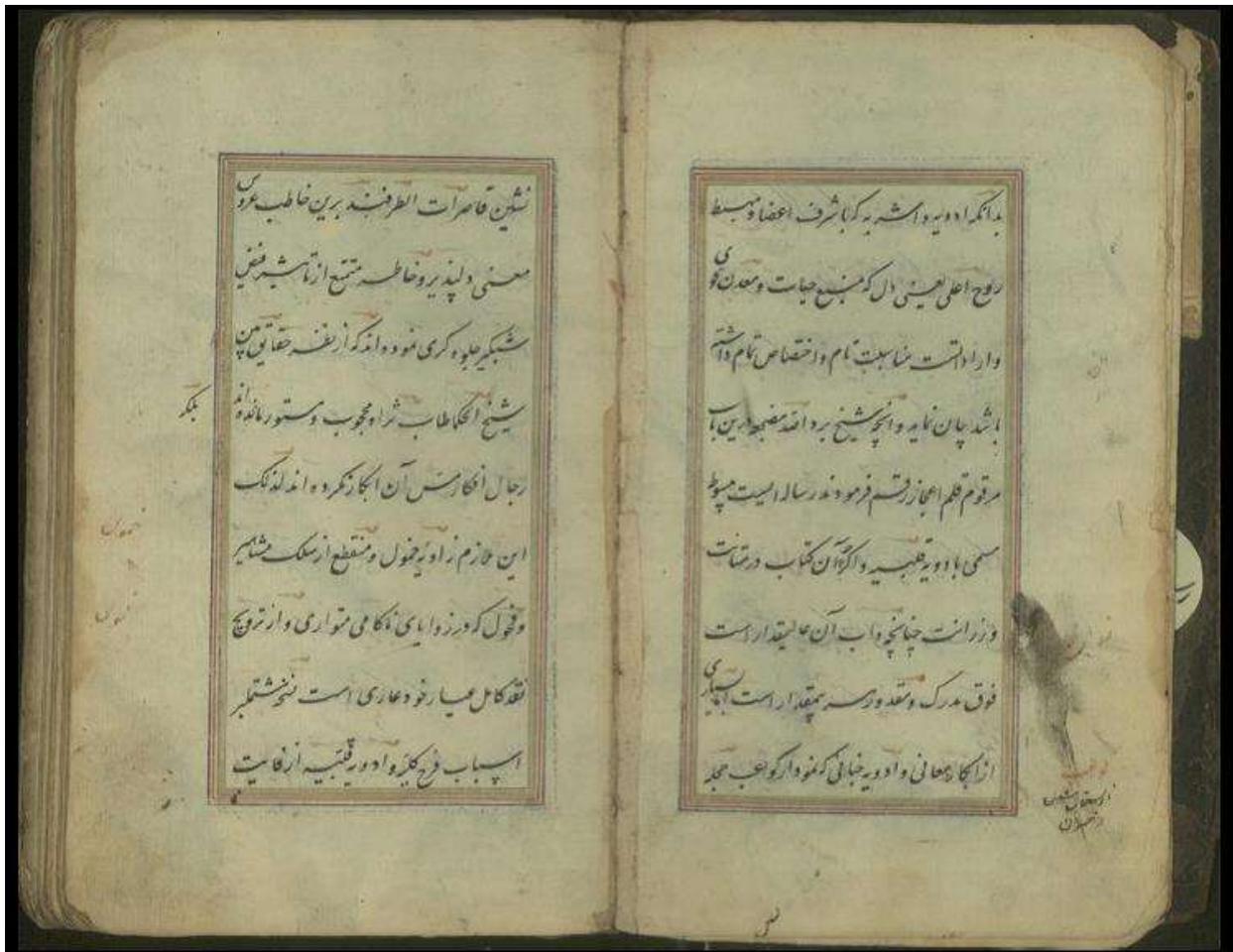


Figure 2: A page of "Kitab al-Adviyat of Qalbiye" (book on drugs for cardiovascular disease) by Avicenna (Majlis library)

Sleep disorders, memory disturbances, dementia, Alzheimer, hallucination, illusion, mania, melancholia, nightmare, love sickness and sexology are examples of 19 neuropsychiatric conditions mentioned by Avicenna in Canon of Medicine. Avicenna commented on a close relationship between the psychological and physical conditions of his patients Ibn Sina. (1997).

Even though some previous surveys discussed about melancholia in Persian medicine Dalfardi *et al.* (2014), this study is the first survey that has focused profoundly on all aspects of depression and sadness from Avicenna's point of view insisting on prevention and treatment.

The exact history of depression has not written yet. In fact, its medicalization has been formed after nineteenth century Rousseau. (2000).

The aim of this study is to introduce Avicenna's ideas on neuroscience and psychiatry, focusing on depression.

Materials and methods

This is a narrative review with focusing on the history of medicine which explains the relationship between depression and old descriptions of the disease. The

explanation of depression in the *Canon of medicine* was done with searching some terms like "Sadness" and "unhappiness" in this book. After this review, the modern medicine texts and databases evaluated for comparison of these results with Avicenna's point of view on depression.

Results

Historical Perspective

Psychiatry has long root in the Persian history. Zoroastrianism named for its messenger, Zoroaster is one of the eldest religions in the world. It has a privileged history and was the dominant religious tradition of ancient Persia before Islam (before 637 CE) Dhalla. (1938).

Avesta, the holy book of Zoroastrians (dates back to at least 3000 years ago) explained prahaoma syrup which was made by Ephedra distachya L. It was the first known euphoriant antidepressant drug in the history Najmabadi. (1996). Also, psychiatrists were mentioned as a main group of physicians, called mansrspand baešaza. Later, there was a psychiatric drug in the Sassanid era, named "happiness drug". The happiness drug was a psychotherapeutic strategy represented as a medicinal

compound in a Pahlavic manuscript from the Sassanid period (224-637AD). It contains moralist recommendations for better life fulfilled with happiness, far from sadness and patience mortar Ji, Ji, & Assana. (1993), Stausberg. (2008), Zargarani *et al.* (2012).

Also, depression has a long history in Greek medicine. Melancholia seems to be the oldest term described depression. All over the history of medicine, melancholia was introduced with various definitions and manifestations Dalfardi *et al.* (2014). The term of melancholia is originated from two Grecian words "Melas" and "Chole" that mean "black" and "bile" respectively Nolen-Hoeksema. (1990).

According to Hippocratic (460-370 BCE) literatures, black bile causes a wide range of symptoms, that the main ones in the field of psychopathology is fear "Phobos" and depression (dysthymia). However, the psychological association of black bile with depression and anxiety had an important role in originating the concept of melancholia. On the other hand, Celsus (42 BCE-37 CE) described melancholia as subtype of madness (insania). He believed that melancholia was affairs of depression (tristitia) that caused by black bile. He mentioned both physical and psychotherapeutic methods for patients Ahonen. (2014). Unlike previous scientists, Plato (427-347 CE) did not associate melancholia to the black bile and described "Melancholikos" for the patients who were unable to think Tellenbach. (1980).

Aristotle (384-322 CE) associated melancholia with novelty and wit and believed that inappropriate amount of black bile caused melancholia Pies. (2007). Manifestations of melancholia according to the Aerates of Cappadocia were as follow:

Significant sadness, Stagnation, Tranquility not related to fever Kotsopoulos. (1986).

He linked melancholia and mania as two symptoms of one disorder Marneros. (2001).

Depression in the Avicenna's Books

Although there is not exact term of "Depression" in different books of Avicenna, but according to the various symptoms and diseases such as "Melancholia", sadness and also treatments based on exhilaration of patients, probably a relation between concept of depression in allopathic and Persian medicine can be established. From this view firstly, we explain disease and symptoms which can be related to depression according to Avicenna.

Definition and etiology

In one of his publications titled "Kitab al-Adviyt-ol-Qalbiye", Avicenna defined happiness, and different aspects of sadness. According to Avicenna, the heart is the origin of different kinds of spirits and souls. He believed in a significant relationship between depression and various types of diseases. He also mentioned that convalescents, thin and cachectic patients, women and the elderly, are at greater risk of depression Ibn Sina. (2009).

In the doctrine of Persian Medicine (PM), the influence of the emotional status on human's health is more acute than other factors and it seems to induce drastic changes Jorjani. (2002).

Avicenna determined that emotional responses could cause particular medical illnesses. He was the first who introduced the benefit of music on emotional distress. He maintained that a combination of humors could cause depression, which could be consistent with transmitter regulated mechanism of depression Namazi. (2001).

He associated melancholia with the brain and asserted that the main reason for its development is an excess of black bile in the brain. He also stated that it is not unlikely that melancholia originates from the heart. To justify this theory, he stated that corruption initially occurs in the heart and consequently the brain is affected and then is transferred through blood from the heart to the brain. However the reverse condition of the aforesaid status is also probable Yousofpour *et al.* (2015), Some clinical and cross-sectional surveys have proved the relationship between depression and heart disease despite the fact that the heart disease is not accepted as the etiology of depression Kang *et al.* (2015), Waloszek *et al.* (2015).

Persian medicine is based on the theory of humors which consists of blood, phlegm, black bile and yellow bile. Moderation in amount of these humors would promote the individual's health. Imbalance of black bile might lead to some disorders in brain and other organs as well Mojahedi *et al.* (2014), Naseri & Ardakani. (2004).

Avicenna defined melancholia as a change of outlook caused by excessive black bile as a natural passage towards corruption. In general and as a key factor, Avicenna associated affection by melancholia with abnormal increase of black bile Yousofpour *et al.* (2015). Based on DSM-V criteria, Major Depressive Disorder (MDD) appears without a history of mania or hypomania episode. Furthermore, this episode must last 2 weeks to be considered as major depressive disorder. Also depressed mood is one of the most important criteria for major depressive disorder Sadock & Sadock. (2015).

He categorized the cause of melancholia according to two categories, intra cerebral and extra cerebral. Intra cerebral etiologies can be attributed to either of the two following, simple cold and wet intemperament and material cold and wet intemperament. In the first group, the substance found in the vessel enters into the brain from somewhere else, but in the second group substances of the brain vessel produce black bile Ibn Sina. (1997).

Different types of melancholia related to extra cerebral sources:

Black bile that distributes throughout the body, Black bile that accumulates in the spleen but it has no ability to clean it, swelling in the abdomen (hypochondria), Swelling in artery occlusion with mesentery vessels (mesentery), Obstruction without swelling, extra cerebral cause of black bile production, while primary substance exists in the

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brain, Extreme sadness or fears are both related to stronger cases of melancholia.

Avicenna attributed the black bile that produced melancholia to normal black bile, phlegm that had been converted to black bile or blood that had been converted to black bile Ibn Sina. (1997). As problem thinking has been included in definition of Melancholia from Avicenna's point of view, and diminished ability of thinking and concentrating is an important criteria for DSM-V, it might be possible to establish a logical relationship between these two definitions Ibn Sina, (1997), Sadock & Sadock. (2015).

Allopathic medicine describes various etiologies for depression such as biological, genetics, psychosocial and environmental factors Saveanu & Nemeroff. (2012). In both approaches they can be categorized as intra cerebral and extra cerebral etiologies. Depression caused by Cold-Wet intemperament. Since cold-wet intemperament leads to decrease of metabolism, and on the other hand, PET scan proves the decrease of metabolism in anterior part of the brain, same etiologies can be concluded for both approaches (Parvinroo *et al.* (2014), Sadock & Sadock. (2015).

Avicenna described black bile, mesenteric artery, obstruction and fear as extra cerebral etiologies generally. Increase of black bile causes changes in sleep pattern Ibn Sina. (1997). In the same way, depressed individuals sleep less and dream more which can be associated with nightmares of black bile Cukrowicz *et al.* (2006). Avicenna introduced sever fear and sadness as the most important factor of affecting Melancholia Ibn Sina (1997).

Clinical manifestation

Avicenna believed that pulse alterations could ensue from emotional conditions, and he specified the particular pulse of different emotional states. Furthermore, individuals who had different emotional responses, exhibited different patterns of behavior according to their specific temperament Mosaddegh *et al.* (2013). In some new researches the relationship between heart rate variability and depression has been proved Brunoni *et al.* (2013), Yeh *et al.* (2016).

Avicenna divided the common symptoms of melancholia into two categories, early phase and chronic phase of the disease. Symptoms of early stage melancholia include suspicions of evil, fear without cause, quick anger, love alone, involuntary muscle movements, dizziness and tinnitus Shakeri *et al.* (2016). In the chronic phase, other symptoms include moaning, suspicion, sadness, fear, restlessness, increased libido and abnormal fear such as fear that the sky may fall on one's head, fear of being swallowed by the earth, fear of tricksters, ruler or thief. Also a person imagines that he is king, fierce, evil or a bird. Imagining things that do not exist, involuntary laughter and affection for death are other symptoms of the chronic stage of melancholia Ibn Sina. (1997).

After describing general symptoms of the disease, he explained each symptom individually. For example, he counted the symptoms related to the increase of black bile specifically in the brain, spleen and stomach Ibn Sina. (1997). Medieval scholars strongly emphasized on relations between depression and the seasons and they believed that the disease is more common during winter and autumn (Jorjani, 2002). Avicenna wrote that mental state is one of the most important of the six essential principles for promoting good health and treatment of disease Ibn Sina. (1997), Kordafshari *et al.* (2014).

The main goal of current investigation is to develop a logical relationship between MDD and Avicenna's melancholia.

Depressed mood and sadness are mentioned as essential and basic criteria for diagnosis of major depressive disorder. Among the symptoms of melancholia, symptoms caused by black bile in the spleen, include increased appetite and sexual desire; consistent with criteria DSM-V, No.3 for major depressive disorder. In the chronic stage of melancholia, a person is affected by restlessness, consistent with criteria DSM-V, No. 5. Frequent thoughts about death and attempted suicide have a close relation with a desire for death in melancholia, as described by Avicenna. Loss of body weight in melancholia is consistent with criteria No.3, DSM-V. Weakness could be associated with criteria No.6, DSM-V Ibn Sina. (1997), Sadock & Sadock. (2015).

Prognosis

Avicenna described the best kind of melancholia which has developed by conversion of blood humor into black bile. He also believed that melancholia presented with laughter exhibits a better prognosis Ibn Sina. (1997). Lack of comorbid psychiatric and personality disorders and also advanced age of first episode are good prognostic indicators of major depressive disorders Sadock & Sadock. (2015).

Treatment and management of depression according to Avicenna's view point

In Avicenna's opinion, the disturbance of humors cause psychiatric diseases and therefore the treatment should concern the balance between humors. The recommended treatment strategies for achieving the result consist of life style modification, medical treatment and manipulation or physical therapy Namazi. (2004).

As claimed by Avicenna, the following items provide mutual and effective treatment for most diseases with no consideration of the causes and the variety of illnesses that might be produced:

Happiness and cheerfulness, Visiting someone whose company is enjoyable (for example a man who was near death from scarcity of love was cured as he saw his mistress), Pleasant smells (aromatherapy), Lovely sounds (music therapy), Also in some cases, traveling to another country and changing the place of residence or season

were thought to be effective treatments of disease. Avicenna emphasized that it is better to treat melancholia in its early stages because treatment becomes much more difficult in the chronic phase Ibn Sina. (1997). Avicenna described psychotherapeutic techniques for treatment of various types of psychological disease Shafii. (1972).

Life style modification

Plans for lifestyle modification should include changing sleep patterns, as well as the climate of living environment, diet, exercise and eliminating bodily waste products. As mentioned above, Avicenna has especially focused on importance of the role of happiness in treatment of depression Ibn Sina. (1997), Rezaeizadeh *et al.* (2009).

Recent studies approved the important role of climate Cho *et al.* (2014), Lim *et al.* (2012), nutrition Kim *et al.* (2015); Sánchez-Villegas *et al.* (2012) and exercise Sarris *et al.* (2014) in depression which has been described by Avicenna 1000 years ago. Mild climate and also living in a house with humid and fragrant weather is suggested. Beyond these, eating energetic, sweet and greasy food which supplies the body humidity is necessary for treatment of depression. It's good for such patients to take a shower before the meal, as pouring lukewarm water over the head makes feeling relaxed. It would be better avoid eating beans, bacon, lentils, cabbage, concentrated wine

and salty, spicy and sour foods too. However normal sexual activities cause happiness, but depressed patients should avoid from hypo sexuality. According to Avicenna's point of view, exercise is exhilarating and induces a sense of well-being. He places a strong emphasis on sporting as the most important contribution for maintaining good health Ibn Sina. (1997). According to PM, sexual intercourse reduces sadness Ibn Sina. (2009) and has a significant role in generating a state of exhilaration Ibn Nafis. (2004).

Medical Interventions and Manipulations

Treatment includes medication and manual operations. Medication includes prescription of exhilarating and medicinal plants that repel the materials which cause depression. These manual operations include massage, phlebotomy and cupping. According to Avicenna, some drugs act by eliminating harmful humors and balancing beneficial humors. Remedies such as "exhilarating" are effective in treatment of depression, by strengthening the heart and creating feelings of happiness. Ibn Sina, (1997), Nozad *et al.* (2016).

According to Avicenna, specific plants and fruits have exhilarated effects. Most of such plants have constituents that affect the brain and heart and some are used to treat anxiety Ibn Sina. (2009) (Table 4).

Table 1: Medicinal plants for treatment of depression from the view of Avicenna and their current effects

Scientific Name Family	Name in PM	Parts Used	Effects in PM	Pharmacological Effects/ Active components	Type of study
Pistacia vera L. Anacardiaceae	Festeg	Fruit	Exhilarating Cardiac Tonic	Regulate HPA axis function Anti-inflammatory/Flavonoids & tannins	In vitro (Hosseinzadeh <i>et al.</i> , 2012)
Coriandrum sativum L. Apiaceae	Kozboreh	Leaf, Seed	Exhilarating Cardiac Tonic Palpitation relief	MAO-B inhibitor/ Linalool	In vivo (Cioanca <i>et al.</i> , 2014, Guzmán-Gutiérrez <i>et al.</i> , 2015, Kharade <i>et al.</i> , 2011)
Hyacinthus orientalis L. Asparagaceae	Sunbul	Herb	Exhilarating Cardiac Tonic Memory Enhancer Palpitation relief	Regulate HPA axis function/Flavonoids	In Vitro(Hosokawa <i>et al.</i> , 1995)
Inula helenium L. Compositae	Rasen	Root	Exhilarating Cardiac Tonic Palpitation relief	Regulate HPA axis function/Flavonoids	In Vitro(Wang <i>et al.</i> , 2012)
Echium amoenum Fisch. & C.A.Mey. Boraginaceae	Lesan-Al-Sour	Flower	Exhilarating Cardiac Tonic Palpitation relief	Regulate HPA axis function/Flavonoids	Human study(Sayyah <i>et al.</i> , 2006)
Terminalia cheb ula Retz. Combretaceae	Halilaj	Fruit	Exhilarating Memory Enhancer Palpitation relief	Anti-depressant like activity/Chebulinic acid	In vivo (Onasanwo <i>et al.</i> , 2014)
Centaurea behen L. Compositae	Bahman	Root	Exhilarating Cardiac Tonic Palpitation relief	Regulate HPA axis function/Flavonoids	In Vitro(Sheikh <i>et al.</i> , 2016)
Doronicum pardalianches L. Compositae	Durunaj	Root	Exhilarating Cardiac Tonic Palpitation relief	-	
Cyperus longus L. Cyperaceae	Soud	Root	Exhilarating Cardiac Tonic		

Crocus sativus L. Iridaceae	Zafran	Flower	Memory Enhancer Exhilarating Cardiac Tonic	Dopamine, norepinephrine & serotonin reuptake inhibition/Crocin & safranal	Human study(Akhondzadeh <i>et al.</i> , 2004)
Lavandula angustifolia Mill. Lamiaceae	Ustokhodus	Herb	Exhilarating Cardiac Tonic Memory Enhancer	Antidepressant-like effects/Flavonoids	Human study(Akhondzadeh <i>et al.</i> , 2003, Basch <i>et al.</i> , 2004)
Melissa officinalis L. Lamiaceae	Badranjbyeh	Herb	Exhilarating Cardiac Tonic Palpitation	Norepinephrine enhancement/Flavonoids & Tannins	In vivo (Emamghoreishi & Talebianpour, 2015, Shakeri <i>et al.</i> , 2016)
Ocimum basilicum L. Lamiaceae	Badruj	Herb	Exhilarating Cardiac Tonic	Serotonergic agent/Flavonoids	In vivo (Abdoly <i>et al.</i> , 2012, Silva, Pezzini, & Soares, 2015)
Cinnamomum camphora (L.) J.Presl Lauraceae	Kaphour	Gum	Exhilarating Cardiac Tonic Memory Enhancer	Regulate HPA axis function/Flavonoids	In vitro(Osawa <i>et al.</i> , 2014)
Cinnamomum cassia (L.) J.Presl Lauraceae	Sazej	Leaf	Exhilarating Cardiac Tonic	Serotonin reuptake inhibitor/Flavonoids	In vivo (Yang, Li, & Chuang, 2012, Zada <i>et al.</i> , 2016)
Cinnamomum zeylanicum L. Lauraceae	Darsini	Sticks	Exhilarating	Antidepressant-like activity Regulate HPA axis function/Flavonoids	In vivo (Emamghoreishi & Ghasemi, 2011, Jayaprakasha & Rao, 2014)
Albizia julibrissin Leguminosae	Abrisham	cocoon	Exhilarating Cardiac Tonic	Increased GABA & Serotonin/Flavonoids	In vivo (Kang <i>et al.</i> , 2000, Kim <i>et al.</i> , 2007)
Ficus carica L. Moraceae	Teen	Leaf	Exhilarating	Regulate HPA axis function/Flavonoids	In vitro(Badgajar <i>et al.</i> , 2014, Mawa, Husain, & Jantan, 2013)
Phyllanthus emblica L. Phyllanthaceae	Amoleh	Fruit	Exhilarating Cardiac Tonic Memory Enhancer	MAO-A inhibitor/Flavonoids	In vivo (Dhingra <i>et al.</i> , 2012, Kumar <i>et al.</i> , 2016)
Saccharum officinarum L. Poaceae	Tabashir	Gum	Exhilarating Cardiac Tonic Palpitation relief	Dopaminergic Regulate HPA axis function/Flavonoids	In vivo (Feng <i>et al.</i> , 2014, Gamberini, Gamberini, & Nasello, 2015)
Polypodium vulgare L. Polypodiaceae	Basfayej	Rhizome	Exhilarating	-	-
Malus domestica Borkh. Rosaceae	Tofah	Fruit	Exhilarating Cardiac Tonic	Regulate HPA axis function/Flavonoids&Omega-3	In vitro(Manzoor <i>et al.</i> , 2012, Tavakkoli-Kakhki <i>et al.</i> , 2014)
Citrus medica L. Rutaceae	Utruj	Rind of Fruit	Exhilarating	Anti-Inflammatory Regulate HPA axis function/Flavonoids	In vitro(Menichini <i>et al.</i> , 2014)
Santalum album L. Santalaceae	Sandal	Wood	Exhilarating Cardiac Tonic Palpitation relief	Regulate HPA axis function/Flavonoids	In vivo (Yan, Liu, & Lin, 2013)
Taxus baccata L. Taxaceae	Zarnub	Leaf	Exhilarating Cardiac Tonic	Regulate HPA axis function/Flavonoids	In vitro(Feucht, Schmid, & Treutter, 2015)
Curcuma zedoaria (Christm.) Roscoe Zingiberaceae	Jadvar	Root	Exhilarating Cardiac Tonic	Regulate HPA axis function/Flavonoids	In vitro(Tariq <i>et al.</i> , 2016)
Elettaria cardamomum (L.) Maton. Zingiberaceae	Gagoleh	Seed	Exhilarating Cardiac Tonic	Regulate HPA axis function/Flavonoids	In vitro(Joanna Brodowska <i>et al.</i> , 2014)
Zingiber zerumbet (L.) Roscoe ex Sm. Zingiberaceae	Zoronbad	Root	Exhilarating Cardiac Tonic	Increase Dopamine/Curcumin	In vivo (Xu <i>et al.</i> , 2005)
Corallium rubrum-	Bosd	Root	Exhilarating Cardiac Tonic Palpitation relief	-	-
Polyporus officinalis-	Garigon	Fruit	Exhilarating Cardiac Tonic	-	-

Some medicinal plants which used as exhilarating in treatment of depression have been evaluated by modern methods and their effects have been proved. The three notable examples of such medicinal herbs are Crocus Sativus Akhondzadeh *et al.* (2004), Noorbala *et al.* (2005), Echium Amoenum Sayyah *et al.* (2006), and Lavandula Angustifolia. Mill Akhondzadeh *et al.* (2003). Some other Persian medicine products show antidepressant effects Nazari *et al.* (2013). In the same way, therapies such as music therapy, aromatherapy and making social contact have been suggested as effective treatments for depression by Avicenna and other scientists of the medieval period.

Discussion

To sum up briefly, except diagnostic criteria's of both major depressive disorder and melancholia, some other common points could be detected in both conventional and Persian medicine about depression. Both emphasize on high prevalence of the disease and the mutual relationship between depression and some other diseases along with the role of sadness and psychosomatic situations that cause several illnesses in Avicenna's point of view. Both Epidemiological studies and Avicenna emphasized on high prevalence of depression in women Ibn Sina. (1997), Kessler *et al.* (1993). Etiological classification of the depression could be categorized as intra cerebral and extra cerebral generally. Herbal medication, happiness, music therapy, aromatherapy, massage, social and familial communications and life style modification are the same treatment methods of depression in both allopathic medicine and Avicenna. Consisting on starting the treatment on early phases of disorder is the other common approach of the disease. According to the above cases and terms of major depressive disorder of DSM-V criteria and since at least five of these criteria are consistent with Avicenna's description, it is concluded that major depressive disorder is the closest disease in modern medicine to the melancholia which described by Avicenna. Also, there are some points in Avicenna's definitions that cannot be defined by current findings. As example, in the book ("Kitab al-Adviyat al-Qalbiye") Avicenna states that sadness and happiness are directly linked to the heart. Accordingly, he states that strengthening the heart is important for treating depression Ibn Sina. (2009). Also, Avicenna presented many treatment remedies and approaches for this disorder. Table 1 shows the medicinal herbs mentioned by Avicenna which might have antidepressant effects. Several factors are associated with the etiology of depression. On the other hand, routine antidepressant drugs with various probable mechanisms such as inhibition of reuptake of serotonin or dopamine would treat the depression Jakubovski *et al.* (2015). Although, there are not any current evidences to prove the antidepressant effects of some of the herbs presented by Avicenna, some other ones contain antidepressant

components according to their pharmacological mechanisms, described in table 1. To the best of our knowledge these medicinal herbs indicate their antidepressant effects in different probable mechanisms. These plant remedies contain a wide range of compounds like flavonoids, linalool Guzmán-Gutiérrez *et al.* (2015) and Chebulinic acid Onasanwo *et al.* (2014) and also omega-3 Tavakkoli-Kakhki *et al.* (2014) have antidepressant effects as well. Some flavonoids like isoquercitrin affect through regulation of HPA axis function Butterweck *et al.* (2004).

Conclusion

Avicenna was one of the scientists that emphasized on prevention as well as treatment in neuropsychiatric disorders. Although major depressive disorder and melancholia or sadness is not exactly the same, but according to their similarities, it can be considered as preliminary definitions of depression in the history. Although, some definitions and medicinal herbs suggested by Avicenna for this disorder cannot be defined by current findings, most Avicenna's definitions and prescriptions are supported by current findings. Most of them are good potentials for further investigations to evaluate in current medicine and may open new horizons in treatment of depression.

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