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Research Article

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Genetic Interpretation of Some Medico- Philosophical Theories of Ibn Sina: 2- Ibn Sina's Theory of Mixtures and Essence

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Abstract

In his pioneering manuscript: Treatise on Cardiac Drugs [Risalat al Adwiya al Qalbiyah], Ibn Sina stated, Each organ has a special structure which is the result of specific mixtures in the essence but this special structure is developed by the cause of the numbers of mixtures and the form of their structure.

In the current study, we traced the linguistic and historical sources for the meaning of the terms "mixtures/akhlat" and "humors", and then we adopted the interpretation of the term "akhlat" as they are the "mixtures/chromosomes", while the term "humors" refers to a wide range of biological molecules; some of them do not apply to term "mixtures/chromosomes.

Ibn Sina, by his scientific intuition, deduced and explained the substantial changes in the embryonic development process, and he was one of the first scientists to predict the existence of the zygote as a drop of blood. Furthermore, Ibn Sina – in contrast to Aristotle – believed that females do produce akin to male semen, which may apply to our current notion of ovum.

With regard to the term essence, Ibn Sina mentioned it in the context of the process of creating the soul and the formation of the embryo as well. Therefore, we adopted the definition of the essence as the first perfection/soul/human genetic core/ zygote, and finally, we explained the inevitable dialectical relationship between the three essential contents of the "essence", which are the soul, the mind and the heart.

Furthermore, the current study proposes that Ibn Sina was the first to deduce and develop the theory that genes contribute to genotype, and the genotype contributes to the phenotype, which is clearly manifested in the causal relationship between the genotype and phenotype in the sense that the phenotype is the gift of the genotype.

Keywords: Ibn Sina, Mixtures, Essence, Genetics, Humors, Zygote.

1. Introduction

This study is the second in a series of studies aimed at explaining and interpreting some of Ibn Sina's medico- philosophical implications from a genetic perspective. In the first study, we explained the genetic interpretation of the theory of the soul creation and we proposed for the first time the term "sacred pairing theory" between blood, soul and genes [1]. Furthermore, we assumed that the soul is likely to have been born directly before- or associated with- the first division of the zygote cell into cleavage.

Galen (AD130-200) used the theory of humors to explain individual differences in character. The four primary humors, *chole* (bile), *melanchole* (black bile), *sanguis* (blood) and *flegma* (phlegm), are related to cosmology theory which states that "fire, earth, air and water are the four basic elements of all things" [2]. According to Galen these humors must remain in balance for a person to remain healthy. The theory of humors was an accepted medical teaching until the Renaissance (Renaissance lasted from the 14th to the 17th century [3].

In fact, the term humors as one of the theories of ancient Greek medicine, is an elusive and ill-defined term. Evidence that, Mones, et al., (2013) revealed that "retrospectively, there are clearly a few missing elements in the Unani medicine that were beyond the knowledge of the time because the science of a thousand years ago could not have resolved them (humors) [4]. One of the most obvious

is the lack of a clear description of the chemical composition of humors. However, Ibn Sina defined humors as a "runny substance" that originates from food; they are carried throughout the body by the blood and used for nourishment and growth.

The word essence (*Lat. essentia*) is related to the Latin term *ens* (being), which itself implies a relationship to *esse* (to be). Essence is what is, what exists. In this sense, it designates a concrete, singular reality in the act of existence. Essence is, moreover, a substantial reality. Essence exists in and of itself; it exists without the aid of a substratum that receives and supports it. (encyclopedia.com) [5].

In other words, the essence is the cause of itself; it is the origin of all other things and the source of all beings.

The ancient Greek sages were the first to research this essence but their research was limited to the physical essence specifically [6].

The theory of the essence is one of the guiding theories in the philosophical thought of Ibn Sina because it reflects and summarizes his vision of existence and essence as a Muslim philosopher.

Ibn Sina divided the essence into five categories, which can be summarized as follows: The first can be described as the essence of latent power and creative transformation. The second is the compound essence, the third is the primary essence or cytoplasm, and the fourth is the human soul. The fifth essence is the "mind" [7].

The main objective of this study was to explain and analyze the concept and the content of Ibn Sina's theory of mixtures and essence by using new genetic and philosophical perspectives, to verify the extent to which Ibn Sina can be considered the first founder of genetics.

2. Materials

1-Appendix 1 "Fig 1" summarizes Ibn Sina's theory in Arabic.
2- Translation of Ibn Sina's theory from its original language (Arabic) [1]

3- Interpretation and Discussion.

3/1-The Theory of Mixture.

3/1/1- The Source and Meaning of the Term Mixture

3/1/1/1- The Arabic Source

In the Arabic language, the term mixtures have different synonyms: First: The plural of the word mixture, which means a composition of two or more things, such as the mixtures of medicine (compound medicine) or colors.

Second, Mixtures means, mixing between two or more things and the new mixture has become impossible to separate [8].

Third: It is what the Arabic language formulated through its linguistic, cultural and scientific heritage around the concept of the body constitution (temperament of the body).

The temperament of the body is what the body is based on of the blood, "two powers" (Al-merrataine), and phlegm," [Lesan al-Arab, Ibn Manzoor: "pages" (4176-4177) - and 4191).

According to the Dictionary of Lesan al-Arab, the literal translation of the meaning of the term "two powers" (al-merrataine المِرَّتَيْنِ) are (The two coiled strands (braid), and/or long, fine, well coiled strands (tightly braided), and/or the power and sharpness of the mind, and/or powerful intensity and proper organs). These entire synonyms mean that (the two powers (al-merrataine in Arabic) symbolizes two strands tightly coiled around each other (DNA) that result in a proper body and a proper mind). Then, it may be concluded that the origin of the term DNA first appeared in the cultural scientific heritage of the Arabic language. More details about this topic will be evident in our next paper entitled: Genetic Interpretation of Some Medico Philosophical Theories of Ibn Sina: 3-Ibn Sina's theory of the temperament.

3/1/1/2- Greek Source (Humors)

The word humor is derived from the Greek word "chymos" and is equivalent in Latin to humor. Its literal meaning is "fluid". The humors, as Ibn Sina defines them, are the soluble substances produced from food and drink by the various digestive processes in the mouth, stomach, intestine, blood, and organs". Ibn Sina follows the traditional Unani classification of humors (blood- phlegm-yellow bile and black bile). These four humors correspond to the major classes of biological molecules that we know today:

- 1-Normal proteins fall under blood humor.
- 2- Unassimilated and incompletely digested proteins fall under phlegm.
- 3- Fats and lipids fall under the yellow bile humor.
- 4- Other classes, such as organic acids, nucleic acids, and metabolic byproducts fit within black bile humor.

However, the Arabic term of humors as used by Ibn Sina and others is "akhlat" which has a different meaning than fluid; akhlat means "mixtures", and although Ibn Sina defined them in general as "liquid substance" this may not apply well to black bile humor and some abnormal humors [4].

The current study understands and adopts the abovementioned interpretation of the akhlat as they are the "mixtures/chromosomes".

From these data, we can conclude that the term humor refers to a wide range of biological molecules; some of them do not apply to mixtures. The word Akhlat in its origin and Arabic source means definitely and accurately mixtures/chromosomes.

This certainly explains why Ibn Sina emphasized in his manuscript, that the mixtures (both fine and dense mixtures) consist of compound staff and never of simple ones [1].

3/1/1/3- The Exact Meaning of Mixtures

Based on the above linguistic definition, we will discuss the concept of mixtures, and what Ibn Sina meant in his distant era.

Ibn Sina's concept of mixtures was mentioned in the context of referring to the process of creation of the soul, as well as his analysis of changes that occur in the genetic material from the moment of fertilization until completion of embryo. Ibn Sina deduced and explained the substantial changes in the embryonic development process as follows: *The embryonic development process is divided into three stages. The first stage is the churning of semen, which is male semen. The second stage is manifestation of a drop of blood*, (which may apply to our current concept of a zygote). *The third stage is the alteration of semen into a blood clot,* (which may apply to our current concept of a blastocyst) *and then into an embryo* (The Book of Animals, lX, 5,172.3-8) [9].

It is noteworthy and interesting that Ibn Sina – in contrast to Aristotle – believed that females do produce akin to semen, which may apply to our new concept of the ovum; however, he stated that, the female semen (ovum) does not possess a generative power as the male semen does.

In these last words, Ibn Sina seems contradictory to himself, because he initially acknowledged his confidence in the existence of female semen, but he denied its generative role in the reproductive cycle. This contradiction may, of course, be due to the clear influence of Geek thought, especially Aristotle at that time.

From the previous scientific data, we can suggest that the mixtures that Ibn Sina talked about are chromosomes: female gamete (egg) and male gamete (spermatozoa), the genetic material of the sperm and egg then combine to form the single cell zygote.

Another piece of evidence that confirms the possibility of the correctness of the mixtures theory was recorded by (Ervin, et al., 2008) who reported that “In humans, the embryo stage is the first eight weeks post- fertilization. At week one post fertilization, the cells undergo extensive and rapid growth” [10].

These findings apply to some extent to Ibn Sina’s assumption mentioned earlier: *This divine flow that alone is capable of transforming power into action, provided that it is prepared for its perfection without apathy or miserliness.*

With regard to the concept of perfection mentioned by Ibn Sina, the science of embryology has proven the correctness of Ibn Sina's perception of this concept, as (Fernando, et al., 2016) reported that blastomere size within the embryo is dependent not only on the stage of cleavage but also on the regularity of cleavage among the cells [11].

On the other hand, the process of arranging blastomeres takes place under precise genetic control (Magdalena, et al.,2021) [12], and (Reiko, K.et al.,2019) [13]. Furthermore, Bruce, Carlson (2019) [14] reported that “One of the early manifestations of embryonic gene expression is the polarization of the blastomeres of 8- and 16- cell embryo, and this process is also considered one of the developmental events that sets the stage for the specification of blastomeres to become either trophoblast or inner cell mass.These are scientific facts of embryology and genetics that may coincide with Ibn Sina’s perfectionism theory specifically (first perfection) [12-14].

It can be concluded that mitosis is a process of cell duplication or reproduction, during which one cell gives rise to two genetically identical daughter cells. During mitosis, the chromosomes bearing the genetic material are reproduced in the nucleus, and then the doubled chromosomes are precisely distributed to the two daughter cells. Each end of the dividing cell receives a complete set of chromosomes before the ends separate [15]. Therefore, mitosis is the wonderful advanced scientific expression of Ibn Sina’s theory of mixing that occurs in the “zygote”.

3/2: Theory of Essence

Since the current study discusses the issue of the creation of the soul as described by Ibn Sina, the concept of essence must be precisely related to the process of creation. Therefore, the essence is the place in which the processes of creation take place. At this crucial and bright moment, cell division multiplies, and specialized cells begin to work consciously, efficiently, and quickly to integrate the expression of functional genes. All these complicated, integrated, and highly organized processes reflect an active and energetic core. For this reason, the zygote, or “human genetic core” can only be considered Ibn Sina's theory of "Essence".

For more detail, we must acknowledge the fact that, the zygote contains all the essential factors for the development and growth of the embryo, and these factors exist solely as an encoded set of instructions localized in the genes/ chromosomes. The genes of the new zygote that are responsible for protein production remain inactive until several cell divisions into cleavage occur. During cleavage, the relatively large zygote directly subdivides into many smaller cells of conventional size through the process of mitosis. These smaller cells, called blastomeres, are suitable as early building units for the future organism" [15].

The abovementioned paragraph proves the validity of Ibn Sina’s theory of the divine flow. The significance and content of this theory can be deduced through a process of transformation of “latent power” localized in both sperm and ova into the real active acts at the beginning of the fertilization process. Additional proof of the theory of "divine flow" is the inactivation state of the genes of the "new zygote to produce proteins until several cell divisions into cleavage”. In both cases, the process of creation may wait for a divine order/soul to complete its cycle, and this can be understood according to Ibn Sina’s theory of “Emanationism” and “first perfection” , which means that (number of bits of

intelligence and souls of planetary spheres emanating from God in hierarchical order) [16]. These findings apply with, and support our interpretation of the starting point of the soul.

The "Essence theory" can also be proven by contemplating and understanding the tight role of functional genes during the precise process of creation that can only take place in the nucleus/zygote (Ibn Sina's essence). At this very moment, it can be stated that the soul is likely to have been born directly before - or associated with - the first division of the zygote cell into cleavage, and that is done by a strict divine flow (order) to transform "the latent faculties/ powers" (germ cells) before fertilization into action (division), exactly as Ibn Sina stated.

With this super rapid vitality process that takes place inside the zygote cell, a logical assumption emerges that the zygote is an "active essence" and not a "passive one". To explain the importance of this assumption, let us say the following: From a purely scientific point of view, the zygote is an active essence, but from the Islamic philosophical point of view, which has a deep consideration for Ibn Sina, we can say that the zygote is a " passive essence" because it is not activated by itself, but rather is activated by divine emanation.

The current study proposes a new definition of the essence, which is the first perfection/soul/human genetic core/zygote.

This very essence is the result of a wise process of divine creation. This is the essence of which the soul is born at the moment of cleavage, and all the organs and features of the new creature (organism) are formed. This comprehensive definition of essence includes all the categories presented by Ibn Sina except "cytoplasm" which is the primary essence according to Ibn Sina.

The definition adopted by the current study depends mainly on two facts:
• The zygote is a genetic core because it is the luminous meeting point of the union of male and female gametes, the basis of which a new cycle of creation begins for an organism.
• The genetic material is the legitimate representative of the concepts of mixtures "chromosomes", and essence "zygote".

Thence, the real essence is "the human genetic core/zygote" resembling, three major contents:

The Soul

which is the main objective equivalent of life, is definitely meaningful, and it is irrefutable proof. In addition, finally, it is up to God. Furthermore, Ibn Sina stated that "the soul is an immaterial substance that is known through its powers (faculties). Accordingly, it is the human rational soul that survives the body after death and is eternal" [17].

On the other hand, Ibn Sina stated that, *"God Almighty created the soul as a carrier of the physic faculties, which represent the conscious and unconscious mind; they reside in the brain, which is the source of their actions: behavioral, voluntary movement and sensation".*

The Mind

Which is the effective co-essence of thinking and logic, consists of a physical part (the brain) and a morally cognitively imagined part (an immaterial substance) of awareness, cognizance, and control. In this respect, Ibn Sina stated that the five internal senses located in the brain are the operations of the soul. [18,19].

The Heart

Which is the effective co-essence of the vital force (motive faculty) of the body, consists of a physical part (the heart and blood) and a morally imagined part (an immaterial substance) of feelings and love. Moreover, Ibn Sina believed that the heart is the source of divine potentialities. in this sense, these potentialities can be considered an embodiment of the inevitable, complementary, dialectical pairing relationship between the soul, the blood, and the homeobox genes, as mentioned previously.

It is worth noting that Aristotle, in his biological works stated that *"the heart is the primary organ in that it is first formed and is the ultimate source and origin of the undifferentiated blood from which the remaining primary organs- liver and brain- and humors emerge"*. On the other hand, Galen stated that *"the liver, not the heart as Aristotle claimed, is the source of blood"*. The current study proved the correctness of Ibn Sina's hypothesis that the blood is the first that is created in the early stage of embryonic development, and the heart comes immediately after.

Through the previous context, we can clarify and explain some philosophical aspects:
• Both the mind and the heart have a physical component, which is the (brain) for the mind, and (blood) for the heart. However, the soul does not possess this physical component.
• The reason for such a condition is that the soul belongs to the absolute sphere of the creator, which enables it to have absolute sovereignty over the body organs. It possesses a special characterization that derives its cause from the absolute creator "God". That is why it gives a part of its molar nature to the mind and heart, but it never takes anything from them.
• The relationship between the soul and the body has always been a cute and controversial issue in all ages, before and after the emergence of Islam. Moreover, Islamic philosophy introduced new theories about the universe, nature, and man, the most important of which is the theory of divine creation, which is the root axis of Islamic philosophy.
• Ibn Sina believed that the soul requires the body only for the acquisition of its "external perfection", not for its very survival [20].
• Ibn Sina's theory of second perfection/ "body activities/genome" may be a reflection of or a completion of the theory of first

perfection/soul/zygote/genes". That is why we can consider him the founder of the theory of "total perfectionism".

• The soul is one of the major manifestations of the theory of divine creation, and as Ibn Sina stated, *"God Almighty created the soul of fine and delicate mixtures",* and therefore it ascends to the high heavens. On the other hand, Ibn Sina said *"God Almighty created the body of dense mixtures",* which means that at the moment of death, the soul leaves the body, leaving the terrestrial realm for the celestial realm, while the body is buried in the earth because they are both of the same physical nature.

• In his classification of types of the essence, Ibn Sina assigned one of these categories by primary essence to "cytoplasm" but he never mentioned the secondary one, and we suggest that this secondary essential essence is the nucleus, or zygote, "human genetic core/essence".

• Homeobox genes, such as Hox and Sox genes, and other genes play a key role in determining cell identity during embryonic development [21]. Now, a question arises: can this genetic fact indicate the possibility of these genes being related to Ibn Sina's concept of "delicate and fine mixtures" that are responsible for the creation of the soul? If this hypothesis becomes correct, then it would be a great reinforcement for the validity of the "pairing theory" between the soul, the blood and the homeobox genes during embryonic development.

3/3- The Theory of Genotype Contributes to Phenotype

Ibn Sina said: ***Each organ has a special structure*** (qualitative mixture/genotype)* ***which is the result of specific mixtures*** (chromosomes/genes/genetic alleles) ***in the essence*** (nucleus/zygote), ***but this special structure*** (qualitative mixtures/genotype) ***is developed by the cause of the numbers*** (amounts) of mixtures (chromosomes/genes/genetic alleles) ***and the form*** (phenotype) ***of their structure."*** * (in brackets is the author's interpretation)

To understand and interpret this theory, it can be stated that: each organ, each body, and each living organism has its own special and unique genetic structure "genotype/genome" that resembles the complete set of the genetic material of the organism.

In diploid species such as humans, two full sets of chromosomes are present, which means that each individual has two alleles for any given gene. If both alleles are similar (AA, for example), this genotype is homozygous. If the alleles are different (AB, for example), the genotype is considered heterozygous. The expressions "homozygosis" and "heterozygosis" are related to the shape or form of the organism (phenotype), and the cause is more related to the effect of genotype on phenotype according to the theory that "the genotype contributes to phenotype" [22].

Due to the crucial importance of the theory that "the genotype contributes to phenotype" in its relation to the homozygosis and/or heterozygosis states, we provide an example from the field of genetic diseases, Siham, S. et al., (2021) [23]. studied the homozygous nonsense mutation of the *WTN10B* gene in a Moroccan family with split hand foot malformation (SHFM) identified by exome sequencing, and they found that many chromosomal loci and genes have been described as associated with isolated SHFM, i.e., SHFM 1 to 6 [23].

They found that SHFM6 is caused by mutations in the *WNT10B* gene. This homozygous nonsense mutation identified by exome sequencing in a large family with split hand foot malformations highlights the importance of exome sequencing in genetically heterozygous entities.

This example reveals to what extent Ibn Sina was full of awareness, knowledge, inspiration, and genius when he deduced and developed his theory of "genotype contributes to phenotype", which is clearly manifested in the causal relationship between the genotype and phenotype in the sense that the phenotype is the gift of the genotype.

From the abovementioned information, we can easily discover that the ancient root of this scientific knowledge lies in Ibn Sina's theory of "genotype and phenotype". Simply, if we replace Ibn Sina's word "mixtures" with the "words" chromosomes or genes or genotype" so that the meaning becomes certain, congruent and identical.

On the other hand, modern molecular genetics has provided additional evidence for the accuracy of Ibn Sina's theory of "mixture number/or number of the genetic alleles" and its basic role in the formation of "special structure/qualitative mixture/genotype", where (Toshimichi and Ken-nosuk, 1991) [24]. where studied the classification of human genes according to chromosome numbers, and they reported that " By analyzing genes mapped on individual chromosomes (thus including genes not yet precisely mapped), we determined whether codon usage differs among chromosomes or not in the following ways First, human genes for which codon usage could be calculated were classified according to chromosome number mainly based on comments in the FEATURE section of GenBank entries".

It may be possible to clarify that, the terms specific mixture "genes" and special structure "genotype" are based on genetic terms because of their distinctiveness and unique characteristics, which are genetic makeup and not anything else. To confirm the validity of this hypothesis, another example of a genetic approach can be added; currently, scientists are debating how regulatory functions are encoded in genomic sequences.

To answer this question, (Kathleen, et al., 2020) [25]. found "specific regulatory tissue genes" responsible for the regulatory function, these "specific regulatory tissue genes" may be what Ibn Sina meant when he formulated and imagined "special structure"(genotype) and "specific mixture" (chromosomes/genes).

There is further genetic evidence that, alkaptonuria (black urine) is

a rare genetic metabolic disease characterized by the accumulation of homogentisic acid in the body, and that affected individuals lack the functional level of an enzyme required to breakdown this acid. Ibn Sina studied this disorder carefully, conducted practical experiments on it and recorded his observations, but the tools available in his day were not sufficient to discover the main cause of the disease. (Quaz, M. Iqbal) [26] Conducted. the same methodology as Ibn Sina, and found the reason, which was a "single autosomal recessive gene".

At this point, it is appropriate to quote Gruner, who wrote, "Advanced of modern sciences in molecular biology, biochemistry, physiology, and pharmacology have not replaced or diminished the basic tenets of Avicenna's (Ibn Sina) system; to the contrary they have replaced to us the need to explain them in light of the new knowledge and find a way to reconcile the two [27].

4- Conclusion

Based on the assumptions presented by the current study, the following can be concluded:

• The ancient Greek philosophy, represented by the Seven Sages and some philosophical schools, was the first to coin the term "essence" and it was intended to refer to the "physical essence".

• After its emergence, Islamic philosophy was adopted by its great scholars, Al-Farabi and Ibn Sina, who adopted the theory of absolute essence "The final efficient cause" and they inferred it to the existence of God "Allah", as they also inferred it to the divine providence of the world through God's continuous action and continuous creation.

• The current study proposes a new definition of the essence, which is the first perfection/soul/ zygote, considering it the human genetic core. This very essence is the result of a wise process of divine creation. This is the essence in which all organs of the new creature (organism) are formed.

• Ibn Sina was the first to deduce and develop the theory that "genes contribute to genotype, and the genotype contributes to the phenotype" which is clearly manifested in the causal relationship between the genotype and phenotype in the sense that the phenotype is the gift of the genotype.

• Ibn Sina was the first to believe that there was a female gamete (egg) equivalent to the male gamete (spermatozoa).

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