



Review Article

Review on Functions of Khilte Safra

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A B S T R A C T

Khilt means mixture, as Souda Safra Balgham and dam are all mixed in blood capillaries. The concept of Khilt was given by Hippocrates, he believed the cause of diseases was changes produced in humour. Safra is considered as one of the four basic humour. It has many important roles in the body as liquifying blood, providing nutrition, and stimulating the intestines. This paper reviews many important functions of Khilte Safra as well as the diseases caused by Safra and covers the psychological as well as the neurological aspect of Safra.

Keywords: Safra, Khilt, Humour, Diseases

Introduction

Akhat/ Khilt/ Humour - Just like the rest of the world, matter is found in three states - solid, liquid, and gas, likewise our human body is made up of these three states:

Arwah-Gas, Akhlaat-Liquid, Aaza-Solid. These three form the human body.¹

Akhlata is one of the seven essential physiological principles (Umoore Tabiyah). They have a place with those essential ideas, which are the distinguishing feature of this great healing art. It is a framework created by our physicians to clarify all the physiological and pathological processes in the human body regarding Akhlata (humours). In Tibbi terms, all Ratubat-Al-Badan (fluids of the body) are called Khilt or Akhlata (humours) attributable to the way that liquids of the body are not a solitary substance but rather these are of various sorts and properties and serve various functions however are intermixed with one another especially in

blood vessels. Consequently, these are called Akhlata or humours.²

Definition of Khilt

All the Khilts including Safra are the moist and fluid parts of the body, which are formed after transformation (of Surat Nauiyah) and metabolism of the ailments, they assist the function of nutrition in growth and repair and the production of energy for the preservation of individuals as well as their species. A right proportion of Khilt, in terms of quality and quantity, and their blend (homeostasis) helps in the development of health and wellbeing, and an incorrect ratio of the same will eventually cause diseases.³

Origin and Digestion of Safra

Origin and metabolism of the four humours including Safra:

The nourishment, growth, and metabolism of the body are all governed by the four humours. They have their origins in the digestive system.



Four Stages in Digestion

The first digestion takes place in the gastrointestinal tract, resulting in the production of chyle, a waste product found in the faeces, or stool.

The four humours are produced during the second stage of digestion, which takes place in the liver. Bile, urine, and perspiration are used to remove waste.

The third stage occurs in the blood vessels and feeds the body's major organs. It removes its waste through urine and sweat.

The fourth stage occurs in tissues, the final step of the four humour into living tissue. The removal of the waste is just like the third digestion as urine and sweat.

All these humours and Safra originate in the liver as follows:

The Sanguine humour, or blood, is the first to emerge, and it receives the largest, most selective portion of nutrients. It is the most common type of humour, and it circulates throughout the body.

Phlegm, also known as the Phlegmatic humour, is the second to emerge and receives the second-highest nutritional contribution. It's also plentiful and gets into the circulation along with blood.

The Choleric humour Safra, or yellow bile, is the next to emerge, and it receives, a small share of nutrients. Lesser in quantity as compared to sanguine and phlegm. Only a little amount of the residue reaches the bloodstream; the remainder is kept in the gall bladder, which serves as its receptacle, to be utilized as required.

The melancholic humour, or black bile, is the last to emerge, and it receives the coarsest, smallest amount of nutrients. It is the least common. Only a little amount of residue reaches the bloodstream; the remainder is retained in the spleen and used when required.

Al-Khilde Safra

All the yellow fluids of the body are known as Safra including those which express the signs and symptoms of Safra. Safra is hot and dry in nature and is also found in a normal and abnormal form.

The natural yellow bile (bilious humour) is referred to as the "foam" of blood, which is bright red in colour. It is light and pungent. The shade of red implies its degree of hotness. Its formation happens in the liver, and then it either circulates with the blood, or passes on to the gallbladder. The first part has two functions:

- It supports the nourishment of those tissues or organs which require a dispersed form of bilious humour, for eg, lung

- It lessens the blood (i.e., decrease surface tension) and thus allows the blood to move through the very minutest of channels in the human body.

The second part has the following two functions:

- It helps in the elimination of a particular portion of the effete matter of the body. Further, it stimulates the muscles of the (lower) intestine and anus, thereby facilitating them to perceive, when it is essential to go to stool
- Nourishment of the walls of the gallbladder. It cleans the food residues and viscous serous humour off from the walls of the bowel

Temperament of Safra

According to Tibbi physicians, Safra is next to Dum and Balgham in superiority and its Mizaj is Haar Yaabis (hot and dry). The liver produces it and stores it in the gall bladder. Bile has a hot, caustic character, as well as a Digestive virtue, or force that binds it to the other digestive fluids of the middle GI tract. Bile accelerates digestion by digesting food, assimilates and excretes lipids and cholesterol, and acting as a natural laxative by stimulating the peristaltic movement of the intestine. It also aids in the browning of the stool. Choleric residues in the bloodstream help in making it thinner, allowing it to pass through the smallest capillaries; they also boost the inflammatory response and function as a surfactant, opening up the lungs and respiratory passageways.

Signs and Symptoms Produced by Safra

Local

- When it regurgitates in the stomach, Safra produces a burning sensation
- While vomiting, it produces a bitter taste in the mouth
- While passing stool, it causes burning of the anus
- When it falls into the intestine, it stimulates the peristaltic movement due to its irritant property, thus, causing evacuation and diarrhoea

General

- It helps in general stimulation and irritation in the body
- Temperament of Safra is hot and dry therefore its signs and symptoms attribute to the heat and dryness of the body
- The patient becomes hypersensitive hyperirritable, nervous and he promptly act to all sorts of stimuli
- Safra increases heart rate, blood pressure, respiration and general body metabolism²

Types of Safra

Safra Al-Kabid/ Safrae Tabai (Liver or Gall Bladder Bile)

This Safra is a complex liquid consisting of a number of

compounds. Few of them are produced with the result of metabolism and since their functions are still unknown these are considered as Akhlate Fazil (excretory products). Some are secretory products and serve a definite function in the body.

Safra is continuously produced in the liver and stored in the gallbladder. It and enters the intestine only at the time of digestion that is when the food is taken. Due to the storage in gallbladder, Safra becomes 5 to 10 times more concentrated and its alkalinity is reduced.

- **Mizaj:** Hot and dry
- **Kamiyat:** 500-1000 mL
- **Kafiyat:** Specific gravity 1.0101-1.011

Colour: Either yellowish-green or red. Carnivorous bile has bilirubin so its colour is golden yellow. Herbivore's bile has biliverdin, so it is yellowish-green.

Taste: Bitter.

Consistency: Viscid and mucoid.

Composition

Inorganic salts like chloride, carbonate and phosphates. Bile salts like sodium taurocholate and sodium glycolate and Cholesterol, lecithin and traces of fatty acids, soaps etc.²

Functions of Liver Bile/ Safra

- It helps the blood to flow through small vessels and capillaries easily
- Some part of Safra goes to the gall bladder and the other into the blood
- Marara (gall bladder) receives Taghzia (nutrition) from Safra
- It is helpful in the digestion of food
- Safra acts as a detergent into the intestine. It washes the viscous secretion from the small intestine
- It provides stimulation for defecation⁶
- It helps in the digestion of iron, calcium, and other mineral constituents of food. Also vitamin D, E, K, A and carotene
- It increases the peristaltic movement of the intestine
- Safra is used orally to remove constipation
- It maintains the pH of ratubat (fluids) in the duodenum and activates the action of the enzyme
- It neutralises HCL acid in the stomach
- The Balgham present in Safra functions as buffer and lubricant
- Neutralising HCL acid by Safra helps to prevent the corrosion of mucous membrane
- Safra (Bile) act as vermifuge
- Safra acts as a disinfectant and antiseptic against certain types of microorganisms
- Safra attenuates the blood and causes it to diffuse through narrow passages⁷

Al-Safra Al Asbi

The second kind of Safra is the one generating general signs and symptoms of stimulation and irritation and functioning at the time of any emergency in the body and emotional states such as joy, grief anger, heat common cold and are manifested by tachycardia, hypertension, increased respiration, erection of hairs, increase body metabolism and excessive heat production and dryness of the mouth. All these signs and symptoms are of Hararat and Yabusat (heat and dryness). These symptoms are produced by several Akhlat (chemical compounds) called catecholamines (epinephrine, norepinephrine, and dopamine), acetylcholine, histamine, certain amino acid, certain peptides and prostaglandins.

Under all the states of emergency in which body and psychic states are deranged such as tension, emotional States namely rage fear etc. and other states of mental irritation, the secretion of epinephrine and norepinephrine is increased. Similarly under bodily strains namely during exercise, cold, hypotension, asphyxia, anoxemia, anaemia of the brain in hypoglycemia and acute pains secretion of these fluids is increased to meet the emergency. Therefore these are called fluids of fear fight and flight.

Thus it can be concluded that near about all these signs and symptoms shown by epinephrine are attributed to heat and dryness produced by Safra.

Norepinephrine: Norepinephrine performs the same function as exhibited by epinephrine except for certain differences in their effects, namely, norepinephrine produce marked bradycardia, cardiac output is slightly reduced, diastolic blood pressure is markedly increased, peripheral resistance is also increased and this result is more powerful in comparison to epinephrine. It does contraction in all striated muscles. It also causes irritability in Azae Nafsaniya (nervous system) like epinephrine.

Acetylcholine (Khalli Safrin): Acetylcholine plays an important role in controlling all somatic and visceral motor activities. It's not only important in this aspect but is also important in emotion, behaviour and other complex function of the brain. It stimulates as well as inhibits the neurons under various situations. Therefore, various effects exhibited by it are attributed to Hararat and Yabusat (heat and dryness) produced by Safra.⁷

Safra' Ghair Tabai

Safra Tabai becomes Ghair Tabai when a few changes take place in it or when some other substances get mixed with it to an extent that changes its quality and quantity.

Safra Ghair Tabai can be of the following types:

- **Safrae Muhiyyah (Vitelline bile):** It's that type of Safra that is mixed with Ghaleez Balgham (tenacious mucus)

- **Safrae Mirra:** The Safra which gets mixed with Raqeeq Balgham (serous type of fluid) and resembles an egg yolk
- **Safrae Muhtariqa:** That bile which is mixed with "Saudae Ihtraqi" or Burnt Sauda
- **Safrae Kurathi:** As claimed by Abu Sahl Masihi this kind of Safra which is produced in the stomach, is dark green in colour, sticky and exhibits Hiddat. Bile of aluminium ascalonicum colour. This kind of Safra is itself oxidised and changes into colour of Kurath (green)
- **Safra zangari (erugenious bile):** It's also like Safra-E-Kurrathi but has a brighter green colour instead of a dark one. Safra itself gets oxidised and changes into colour of zingar (viride)⁸

Any kind of change in humour leads to change in bodily functions thus resulting in disease. However the deficiency of the humour is replenished, besides other factors, depends on the nature of deficiency itself. If a system has a deficiency of single humour then, then that humour itself makes it up sufficiently, and restore the site of deficiency to its normal composition and function. Whereas if the deficiency is multiple, then the major part is played by that humour of which the deficiency is greatest and alone with other factors of deficiency restore the site to its normal composition and function.⁹

Few Diseases Caused by Safrae Ghair Tabai

Yellow Jaundice: The bilious concentration of the blood becomes too high that it can be seen as yellowish pigmentation on skin and conjunctiva of the eye.

Cholelithiasis: The presence of gall stones in the gall bladder or in the bile duct. They are caused by hardening of the excessive cholesterol and are generally yellowish-green in colour.

Hasfe Safravi: These can be found on the especially over the eyelids, mucous membrane, are yellowish colour protuberance. They shouldn't be count in Warm-e-Haar category but belong to tumours.

Basoore Safravi: These are found over the skin and are yellowish colour pimples or pustules due to Safra.

Cirrhosis of Liver: Sometimes the changes in the liver are so much that it changes its normal red colour to yellowish-red colour. The liver becomes weak and its cells start dysfunctioning.

Apart from these, diseases like Bilious vomiting/ Safravi Qai, Safravi Ishaal, Hummiyate Safraviya and Bole Asfar come under Safravi Diseases.¹¹

The Psychological Effect of Khilte Safra

Passions are aroused, provoked, and emboldened by Yellow Bile. It inspires wrath, irritation, aggressiveness, ambition,

envy, jealousy, and courage since it is inflammatory, irritating, and caustic.⁴ Effort has been made every year to explore the role of bile acids outside of those linked with the hepatobiliary system.

Bile Acids in the Brain and their Impact on Neurology

According to WHO and CCRUM standard Unani terminology suggest Safra as the possible English equivalent is bile/ yellow humour/ bilious humour,¹² and bile acid is one of the constituents of bile. As per some recent researches on bile functions, following the ability of primary bile acids in the liver, they are discharged into the gut where they are changed by the activity of microorganisms in the digestive system to start acting as secondary bile acids. The secondary bile acids can also be sulphated and glucuronidated in the liver or gut, and then combined with glycine or taurine. Various enzymatic responses give bile acids a wide range of properties, not just in terms of lipophilicity and hydrophilicity, but also in terms of their capability to bind active receptors. Bile acids have been shown to activate both cell membrane receptors and nuclear receptors.¹³

Farnesoid Receptor - a Nuclear Bile Acid Receptor

Bile acids were recognised as cell signalling mediators after it was found that they are ligands for the nuclear receptor Farnesoid receptor (FXR).¹⁴

Bile acids can bind to and activate the nuclear receptor FXR, which binds to DNA as a monomer or as a heterodimer with other nuclear receptors, once within the cell.

The nuclear complex that got activated binds to FXR response component for control of the gene expression.

Activation of Nuclear Receptors by Bile Acids

Aside from FXR, the pregnane receptor (PXR), vitamin D receptor (VDR), constitutive androstane receptor (CAR), and glucocorticoid receptor (GR) can be activated by bile acids. PXR helps in the detection and clearance of xenobiotics in the body by regulating the expression of several Cytochrome P450 enzymes involved in their detoxification.¹⁵

PXR also increases the manufacture of neurosteroid hormones, suggesting that it may play an indirect role in neuroinflammation and neurotransmission.¹⁶ VDR is found in a range of cells, such as vascular smooth muscle cells, b cells, monocytes, and adipocytes, and is expressed in the bone, intestine, and kidneys.¹⁷

Evidence of Bile Acid Signalling in Brain

A few early studies have demonstrated that bile acids have been identified in the brain in a few studies, and their presence could be due to de novo bile acid synthesis via cholesterol oxidation.

Bile acid levels have been shown to increase during neuropathological situations in humans, such as hepatic encephalopathy, when bile acids have been found to increase in brain tissue and cerebrospinal fluid (CSF) of patients with acute liver failure but not in control patients.¹⁴

Outside of neurotransmission, bile acids may have neurological concerns. In cases, when bile acids are augmented, such as in patients with obstructive jaundice caused by gallstones, hepatic glucocorticoid clearance is inhibited to the point that the Hypothalamic Pituitary Adrenal (HPA) axis is disrupted.¹⁸

Similarly, after Bile Duct Ligation (BDL), the HPA axis has been shown to be suppressed.^{19,20} An upsurge in serum bile acid levels, which can arouse the opening of the blood-brain barrier, is one mechanism by which extrahepatic biliary blockage leads to a repressed HPA axis.²¹ It permits bile acids to enter the brain, where they are absorbed by the bile acid transporter ASBT, which is found in the hypothalamus.²¹ Bile acids, mainly TCA and GCDA, bind to and activate GR once inside hypothalamic neurons, resulting in a reduction in the expression of corticotropin-releasing hormone, a critical regulator of the HPA axis response.

These studies show that bile acids can influence neurotransmission, neuroendocrine responses, physiology, and neurogenesis, implying that these signalling mediators play a substantial role in neurological function.

Conclusion

Therefore, we conclude that Safra has many functions in the body and they are not precisely a part of liver and GIT functions but many new kinds of research suggest their function in the nervous system as well. Further, any deviation from the physiological nature of Safra leads to imbalance and disease.

Conflict of Interest: None

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