



SIDDHAR THEORY SAARAM (CHYLE) TO SUKILAM (SEMEN) LEADING TO NEWER PROSPECTS FOR MALE INFERTILITY TREATMENT



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Abstract

The seven basic constituents that forms the physical body as per siddhar theory are *saaram*- chyle, *seneer* (blood), *oon* (bone), *kozhupu* (cholesterol), *enbu* (bone) ,*moolai* (bone marrow) and *sukilam* (semen). According to siddhar theory the seventh constituent semen is formed in males by the essential parts of marrow the sixth constituent elements of the body mixed with blood, it is the support of the body and the root of pregnancy. In the recent research, the formation of the early stage sperm cells from the stem cells isolated from the bone marrow is analogous to the siddhar theory. In general these stem cells from the bone marrow would grow into the different cell types in muscle tissue. Early-stage sperm cell has been created from human bone marrow. If mature sperm developed, could be used in the treatment of male infertility. In clinical implications it is important to establish the methods to preserve stem cells and to restore fertility.

INTRODUCTION

According to Siddha physiology the human body is composed of 96 *Thathuvam* or basic principles. Among them, the five *pancha bootham* (primordial elements) are essential¹. The physical constituents which are identical to the various types of tissues are called as *udal thathus* (body constituents). They are also constituted by these five elements.

Five primordial element

Prithvi - Earth

Appu - Water

Theyu - Fire

Vaayu - Air

Aakayam - Space

These constituent's are mentioned in the poem of *Thirumanthiram*².

“RATHAM MUDHALANA EZHUTHATHU
MOONRIN,

URIYA THINATHIN ORUPUR PANIPOL,

ARIYATHULI VINTHU VAAGUMAEL
MOONRIN,

MARUVIA VINTHU VALARUMKAAYATHILAE.

Seven body constituent

Saaram - Chyle

Seneer - Blood

Oon - Bone

Kozhupu - Cholesterol

Enbu - Bone

Moolai - Bone marrow

Sukilam/suronitham - Semen/Ovum

These constituents should be in harmony and normality. Any variation in them will lead to their functional deviations.

Normal function of the seven body constituent

Saram - Gives mental and physical perseverance

Senneer - Imparts colour to the body, nourishes the body and is responsible for the ability and intellect of an individual

Oon - Gives shape to the body according to the physical activity and covers the bones

Kozhuppu - Lubricates the joints and other parts of the body to function smoothly

Enbu-Supports the frame and responsible for the postures and movements of the body

Moolai -Occupies the medulla of the bones and gives strength and softness to them

Sukkilam/suronitham- responsible for reproduction.

According to *Siddhar Theraiyar* the essence of the food becomes,

Saram - same day

Senneer - second day

Oon - third day

Kozhupu - fourth day

Enbu - fifth day

Moolai - sixth day

Sukilam/Suronitha - seventh day

The fusion of these *sukkilam* (semen) and *suronitha* (ovum) constitutes the human body³.

This study is to establish the analogous of siddhar theory with the clinical implication of mature sperm cells from bone marrow in male infertility.

Relation between these body constituents

Constituent is forming part of a whole component. It is the component that is added to something to improve it. Something determined in relation of something that it includes it⁴. Here the relation is between *saaram* to *sukilam* in the manner that, most of them are water components, alkaline in nature and one constituent is formed from the other.

Measurement of water component of the body

Chyle – 9 *Anjali*

Blood – 8 *Anjali*

Musculo fluid – 3 *Anjali*

Fat – 2 *Anjali*

Bonemarrow – 1 *Anjali*

Semen- ½ *Anjali*

When two palms are held together to form a bowel like structure, its capacity is one *Anjali*³.

In spite of continuous production of acids in the body, the concentration of free hydrogen ion is kept almost constant at a pH of 7.4 with slight variations⁵. The pH

level of vital organs in the body should be at 7.365 slightly alkaline to function properly. To defend our body from in excess of acidity, the buffer system that stores alkaline work's hard to neutralize the acid⁶. Chyle is Alkaline due to the content of bile & pancreatic juice. Due to ferment working in the stomach, food that is transformed into a highly volatile acid named cremor; which in turn transformed into a substance rich of volatile salts named as chyle. Chyle is turned into cruor a blood without spirit in the liver, which is imbued with a volatile alkaline salt⁷. Chyle is an alkaline, odorless, milky fluid and contains protein, lipid's (mostly triglyceride) and cells consisting mainly of lymphocytes⁸. Blood is slightly alkaline and its pH is 7.4.^{9,10} By the group of nerve cells located in the medulla oblongata, the pH of blood is closely monitored within a very narrow range (7.3 to 7.5) in order to have normal-body biochemistry¹¹.

During resting condition the muscle is alkaline with the pH of 7.3. Throughout the muscle contraction owing to dephosphorylation of ATP to ADP, the pH of the muscle becomes acidic. The muscle reaction once again becomes alkaline,

during the later part of muscle contraction, when ATP is resynthesized from creatine phosphate. At the last part of the muscle contraction, owing to the formation of pyruvic or lactic acid, the muscle reaction yet again becomes acidic¹². The body produces extreme amounts of cholesterol to counteract large amounts of acids in the blood stream, prior to they damage the living cells. Body produces fat to trap and neutralize acidic waste. Fat in fact is saving the life¹³.

Alkaline balance is essential for Bone health¹⁴. Current research put forward to maintain the proper pH level in the blood which is the principal factor in maintaining on the whole of bone health, with calcium playing a supporting role¹⁵. Bone marrow stroma comprises a variety of cell lineages together with adipose, bone, cartilage, and reticular cells. Alkaline phosphatase have been expressed as a marker for the osteogenic stromal lineage in many previous studies¹⁶. In regarding osteogenesis markers, the production of high levels of the tissue non-specific isoform of alkaline phosphatase is the hallmark in distinguishing osteogenic cells in culture. The significant value of alkaline

phosphatase in bone formation is due to its ability to regulate mineralization of bone matrix¹⁷.

The alkaline pH of semen temporarily neutralize the vaginal secretions during coitus¹⁸. The consensus pH value of semen is of 7.2, as a lower threshold value. Semen sample with less than 7.0 pH, with low volume and low sperm numbers indicates ejaculatory duct obstruction or congenital bilateral absence of the vasdeferens. High pH values may offer little clinically useful information¹⁹.

Semen's alkaline pH is preserved due to spermine, spermidine, foul-smelling putrescine and cadaverine which is present in alkaline pre-ejaculatory fluid secreted by the pea-sized cowper's gland. Seminal vesicles secrete important quartet of amines. Sperm cells are susceptible to acid since their cells are little more than naked genetic nuclei, and if the pH is low it will denature the DNA. The pH of the vaginal fluid's normally ranges from 3.8 to 4.5. Following male ejaculation, the semen's amine bases defend the sperm cells from neutralizing the H⁺ from the acetic acid²⁰.

Formation of the body constituent

SAARAM – CHYLE

The function of the mouth is the ingestion of the food materials. When food is mixed with saliva bolus is formed which is transferred to oesophagus. The peristaltic movement of stomach mix the bolus with gastric juice and convert it into the semisolid material known as chyme⁵. When chyme opens in to the duodenum, it mixes with the bile & pancreatic juice and another significant change is effected. The chyme is no longer chyme, it has lost its uniqueness & the result is a milky fluid called chyle which is intended to become blood²¹. This portion of the alimentary substance created in the duodenum which has already or is about to become albumen will represent a part of the future blood²²

SENEER – BLOOD

It is evident that the materials of the blood must be the derivative of our food. The milky chyle, imbibed by cells is passed on to the lacteal vessels and then conveyed in to the blood. In the lungs it is ventilated & vitalized.

Digestion takes place in stomach

Chymification in duodenum

Chylification in lacteals

Sanguification in pulmonary blood vessels

Sanguification is the production of blood, specifically the change of the products of digestion in to blood²².

The Chyle moves along the lacteals (chylous absorbents) where it is filtered through their gland, is emptied in to the thoracic duct and then it is poured in to the blood of the veins about the base of the neck and is passed by the current of the blood all the way through the right side of the heart, along the pulmonary artery towards the lungs. While the chyle is passing through the chylous absorbents, it undergoes a modification, the nature of which is not understood, but it is a modification which advances it to another grade closer to the character of blood. Chyle is present in blood. Chyle that reaches the lungs is then open out, to the action of the air. By the virtue of the air in the lungs, chyle has acquired the colour and all the qualities and properties of the blood. In a nutshell, it has become blood itself²¹. The milkiness of the serum is accredited to the existence of unaffected chyle in the blood²³.

OON – MUSCLE

Fetal blood-borne growth factors via secondary myofiber may modulate muscle fiber formation forming myoblasts during development. Alterations in serum growth-factor profiles had been assessed by researchers with myoblast cultures as a bioassay²⁴. The Skeletal muscles constitute 75% of water, 20% of proteins & 5% of organic substances other than protein & some inorganic substances. Myosin, Actin, Tropomyosin, troponin, Actin, Titin, Desmin, Myogen and Myoglobin are the muscle protein⁵.

Actin & Myosin are the proteins directly involved in the muscle contraction. Myosin helps in splitting ATP which is the initial event and source of energy in the process of muscle contraction. ATP for this purpose is derived mainly from the oxidation of carbohydrates, fats & aminoacids. Glycogen is found in large amount in liver & muscles. Muscle glycogen breaks down during muscle contraction & produce ATP to supply energy for contraction. At the end of glycolysis glucose-6-phosphate is produced. This G6P can continue on the glycolysis pathway & be used as fuel. Under

aerobic conditions the endproducts of glycolysis is pyruvic acid²⁵. Myoglobin is a cytoplasmic hemoprotein, chiefly found in skeletal and cardiac muscle, which is capable to reversibly combine with oxygen and aid the diffusion of oxygen²⁶. Oxygen from the red blood cells combine with myoglobin and convey it to the mitochondria of muscle cells, where it is used to create energy²⁷.

KOZHUPU – CHOLESTEROL

Glycogenolysis which takes place in muscle produce G6P which continues on the glycolysis pathway and produce pyruvic acid. Pyruvic acid further yield acetyl CoA which is the initiator of citric acid cycle and for the synthesis of cholesterol all the carbon atoms are derived from it. Formation of Acetyl CoA takes place in Mitochondria. Cholesterol synthesis takes place mainly in the liver, also in adrenal cortex, intestine, aortic & arterial tissues. But liver contributes to the synthesis of about 1- 1.5 gm of cholesterol per day & other extra hepatic tissues contributes about 0.5 gm per day²⁵.

ENBU – BONE

The probable precursor of androgens is either acetate or cholesterol. They give rise to the intermediates pregnenolone, which is also the precursor of the adrenal cortical hormone. It is converted to progesterone which leads to the formation of testosterone. Vitamin D3 is the natural form of vitamin D which occur in man & animal. 7- dehydro cholesterol is converted to its active form, cholecalciferol by irradiation of skin²⁵.

Bone is a extremely metabolically active tissue. The progression of osteoblastic bone formation & osteoclastic resorption are constant throughout life which ensures that normal bone structure is maintained. Steroid hormones at any stage can control bone remodeling in a number of ways in the course of the remodeling cycle. They can proceed directly on osteoblast & osteoclast to modify both bone resorption or bone formation. Steroid hormones modify cellular differentiation, proliferation and regulates the expression of osteoblast target genes, for instance such as encoding alkaline phosphatase (AP), osteopontin & osteocalcin. The effects on calcification, matrix production and cell migration, have been explained. Oestrogen is the hormone

which is most directly connected with effects on bone. Androgens and progesterone play's a significant role in the protection of bone structure. For the growth, maturation and maintenance of the skeleton oestrogen is important. Androgens maintain's normal bone structure. Clinical studies using progesterone management suggest protective effect on bone mass. Vitamin D is essential for usual bone development & deficit is related with ricket in children & osteomalacia in adults ²⁸.

MOOLAI – BONEMARROW

Bones are not solid, but are made up of two different regions. It has outer hard, compact and calcium based weight bearing area. It surrounds a network of fibrous bone well-known as cancellous tissue. The Inner region or marrow is situated within the bones which is one of the largest organs of the body. Inner region fills the shaft of the long bones, the trabeculae and extends in to the bony canals which hold the blood vessels. The marrow contain's fluid, fat cells, blood vessels, fibrous tissue & Hematopoeietic cells. Marrow appear yellow when it holds fat cells; red when it has more hematopoeietic cells. The marrow

is the primary site for hematopoiesis. Blood cell that occupy the arteries & veins are produced and mature within the bonemarrow. They are derived from Hematopoeietic cells called stemcells. Stem cells constantly divide to form new cells ²⁹.

SUKILAM – SEMEN

Semen is formed in males by the essential parts of marrow the sixth constiuent elements of the body mixed with blood. It is the support of the body and the root of pregnancy. In the same manner ovum is formed in the female & discharged with the menstrual fluid if not fertilized ³⁰. The formation of the early stage sperm cells from the stem cells isolated from the bonemarrow is analogous to the siddhar theory.

Stem cells are characterized by the capability to restore themselves through mitotic cell division and differentiating into a various sort of specialized cell types. They are cultured from the patient's own tissue and then injected back into the body. To extend healthy longevity and to repair some of the damage caused by aging, organ by organ, regenerative medicine will assist ³¹. Bone marrow or the peripheral blood is

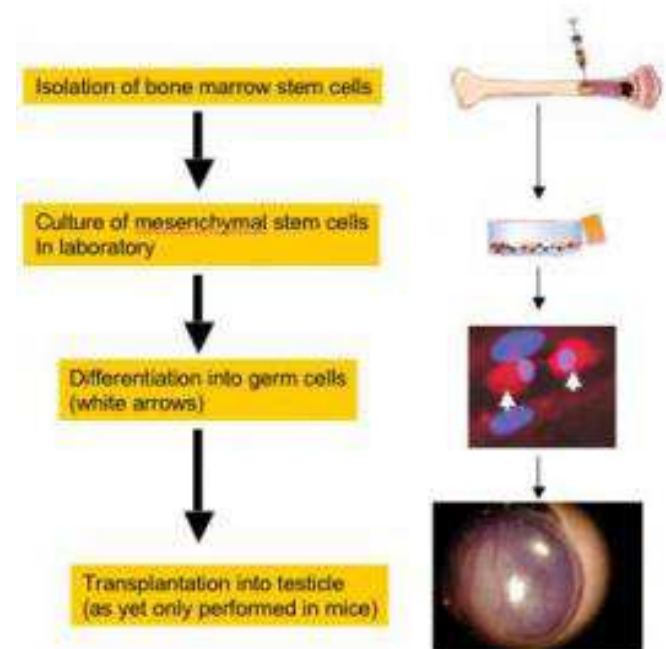
the most common source of stem cells³². The hematopoietic stem cells originating in bone marrow are the first adult stem cells to be used successfully in therapy³³.

Recent research shows early-stage sperm cells has been created from human bone marrow. In the experiment mesenchymal stem cells were isolated from the bone marrow from male volunteers

These cells have formerly been established to develop in to other body tissues such as muscle. They cultured these mesenchymal stem cells in the laboratory & coaxed them to become male reproductive cells, which are scientifically identified as germ cells.(fig 1) Genetic markers showed the existence of partially formed sperm cells called spermatogonial stem cells, which is the early phase of the male germ cell development. Mature sperm if developed ,will be used in the treatment of male infertility³⁴.

Fig 1

How Prof Nayernia and his team cultured from human bone marrow. (Credit: Newcastle University, England



The cellular and molecular mechanisms controlling stem cell role is essential to the hope of stem cells in regenerative medicine, in addition to in understanding aging, tumor formation and gametogenesis³⁵.

Changing of stem cells types from pre-muscle to pre-reproductive cells observed by the researchers is known as Trans-Differentiation. In general these stem cells from the bone marrow would grow into the different cell types in muscle tissue. However the researchers induced a small number of them to grow into spermatogonial cells which is found in the testes which would in general develop into

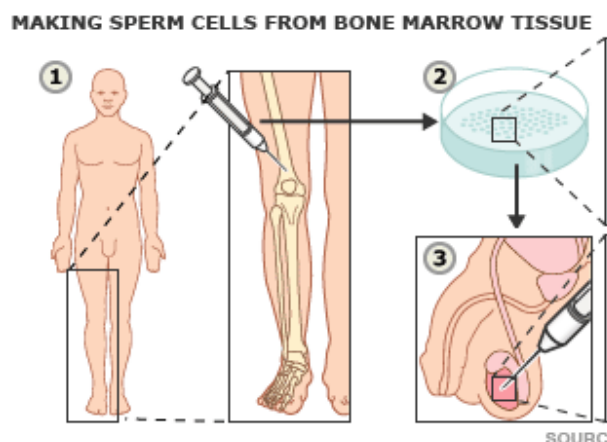
mature sperm cells. According to the research study, stem cells are isolated from the bone marrow of male donors. In laboratory it is cultured and identified. Some of them were induced to develop into spermatological cells, which normally become sperm cells (fig 2). Transplantation of cells into testicle were so far performed in mice³⁶.

general the kind of patients who may make use of the technology are infertile men with azoospermia, Sertoli cell-only syndrome or cryptorchidism and men with cancers who are not able to ejaculate. This will make them propagate their own genetic line rather than using the donor sperm available³⁷.

In clinical implications it is important to establish the methods to preserve stem cells and to restore fertility³⁸. Transplantation of spermatogonial stem cells from infertile donor to a accommodating testicular environment will restore fertility and result in descendants with the genetic makeup of the infertile donor male³⁹.

Knowledge of the impact of different conditioning regi-mens used in bone marrow transplantation on spermatogenesis is important in pre-BMT (Bone marrow transplatation) counselling for the reasons in which the young patients are concerned with their subsequent fertility, number of diseases that compete therapeutic options which may affect spermatogenesis seriously and the necessary of cry-opreservation after

Fig 2



Stem cells will be used to restore fertility in males if banking is established which is similar with regular clinical practices in bone marrow transplants. Advances in reproductive technology had brought new potential for patients not capable to have children normally. In

diagnosis and prior to any treatment in which spontaneous recovery of spermatogenesis is rare⁴⁰. If Immature sperm cells have been created from stem cells in human bone marrow they might one day lead to treatments for male infertility. Infertile men might one day be able to use stem cells in their bone marrow to produce viable sperm⁴¹.

DISCUSSION

Seven body constituents as per siddha physiology has relation of something with one another. In the recent research the formation of the early stage sperm cells from the stem cells isolated from the bonemarrow is analogous to the siddhar theory. Researchers are making an effort to ascertain the association between bone marrow and sperms. When food is ingested it transforms in to chyle which in turn is transformed into blood. From the blood the RBC's carries oxygen and supplies to the

muscle cells. The muscle cells utilizes oxygen to break down the glycogen present in it, during muscle contraction & produce ATP to supply energy for contraction. The end product of this glycolysis is pyruvic acid. Acetyl coA which is formed from the pyruvic acid supplies the carbon atom for the synthesis of cholesterol.

Cholesterol is the precursor in the formation of steroid hormones and vitamin D which are responsible in maintaining bone structure and development. The bone marrow which is one of the largest organs of the body is located within the bones. Bone marrow is the source of stem cells. Stem cells continuously divide to form new cells. Early-stage sperm cells has been created from human bone marrow. Mature sperm if developed, could be used in the treatment of male infertility. In clinical implications it is important to establish the methods to preserve stem cells from bone marrow and to restore fertility.

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