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Review Article

UNDERSTANDING *DHATU POSHAN NYAYA* IN THE LIGHT OF STEM CELL THEORY

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ABSTRACT

The word *Dhatu* forms with '*Dha*' and suffix '*tin*'. It means basic element which helps in construction. A living body comprises of 7 *Dhatus* (tissue), which not only does *Dharan* of the body but also provides *Poshan* or nutrition to the next forming *Dhatu*. Tissue nutrition is the continuous process which persists throughout the life, but it's different during different phases of life. *Acharayas* postulated theories of tissue nutrition and transformation of tissue nutrients into bodily element through *Dhatu Poshana Nyaya* (tissue nutrition and differentiation theory). The theories of tissue nutrition are *Ksheera Dadhi Nyaya* (Law of Transformation), *Khale Kapot Nyaya* (Law of Selectivity), *Kedari Kulya Nyaya* (Law of Transportation) and *Ek Kaal Dhatu Poshan Nyaya* (simultaneous supply of nutrients to whole body). This review is an attempt to explore the Ayurveda's view on tissue differentiation along with physiological and clinical significance of theories of tissue differentiation in a scientific mannery.

INTRODUCTION

In Ayurveda, *Acharaya Sushruta* stated that '*Doshadhatumalammoolam hi Shariram*' i.e., human body is composed of *Dosha* (bioenergies that regulates bodily function), *Dhatu* (structural component) and *Mala* (waste products), which are continuously nourished by *Aahar* (food). This *Aahar* is acted upon by *Jatharagni*, which convert it into *Ahara Rasa* and *Ahara Mala* (urine and stool). This *Ahara Rasa* is still *Vijatiya*, therefore, cannot be absorbed by bodily elements. *Bhutagni* acts on it and make this *Ahara Rasa Sajatiya*. Now this *Ahara Rasa* is acted upon by *Dhatwagni* likewise- *Rasadhatvagni* when act on *Ahara Rasa* divide into *Sthoolabhaga* and *Sukshmabhaga*. *Shoothlabhaga* nourishes the *Rasa dhatu* whereas, *Sukshmabhaga* again divided into *Rakta Nirman Ansh* (which further nourishes *Rakta Dhatu*), *Updhatu* (*Stanya* and *Artava*) and *Mala* (*Kapha*) so on.

The nutrition and differentiation of tissue is different during different phases of life. During intrauterine life, initially (before 8th week of gestation) the nutrition of embryo is histotrophic, whereas after formation of placenta nutrition is haemotrophic. Histotrophic nutrition under a low concentration reduces the risk of free radical mediated damage. Later on, when fetal requirement of O_2 rises, transition to haemotrophic nutrition as establishment of maternal placental circulation occurs. And after birth nutrition is totally enteral means i.e., nutrients are taken in the form of food via mouth. In the same way the tissue differentiation is not same during all phases of life, it follows a certain rule of differentiation. So, this article is an attempt to understand the differentiation of tissue by means of *Dhatu Poshan Nyaya.*

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AIM AND OBJECTIVES

To explain the concept of *Dhatu Poshan Nyaya* through stem cell theory.

MATERIAL AND METHODS

Various Ayurvedic *Samhitas* and modern text are used to find out the association between different sciences on the related topic.

Tissue Nutrition

Tissue Nutrition during Intrauterine Life

As per *Acharaya Charak Sharirsthan* 6th chapter *Ahara Rasa* of mother gets divided into 3 parts – one part nourishes mother's body, one goes in the

formation of *Stanya* and one part nourishes to *Garbha*. During organogenesis, manifested and non-manifested organs get nourishment by the process of *Upsneha* (filtration) and *Upsveda* (percolation/secretion). Vessels (*Dhamani*) of maternal body which carry the nutrients (*Rasa*), runs laterally and longitudinally in all directions through it tend to provide nutrition with their *Upsneha*. As per commentator *Indu* (*Ashtang Sanghra Sharirsthan* 6) consider *Upasneha* and *Upsveda* as *Snigdhatava* and *Utkleda* i.e., becoming wet and moist respectively. Unctuous part of amniotic fluid such as lipid or glycogen contents which causes growth and development of the body (unctuousness similar to *Sneha*) while water and electrolyte content of the amniotic fluid as *Upasveda*.

After completion of organogenesis, it gets nourishment by the process of perfusion, majorly through the umbilical cord and sometimes through the hair. *Acharaya Sushruta Sharirsthana* stated that *Garbhanabhinadi* (fetal umbilical vessels) is attached to umbilicus of fetus on one end and placenta on the other end. Placenta connected with the heart of mother through the *Rasavaha Nadi* (blood vessels)

According to the modern science developing fetus get its nutrition from the secretion of the endometrium or from yolk sac before the formation of placenta and later from the umbilical vessels attached to placenta. As initially nutrition is histotrophic, trophectoderm phagocytosing first oviduct and then uterine secretion called uterine milk. Uterine milk contains glycol protein and amino acid, these are important source of nutrients during organogenesis, when metabolism is essentially anaerobic. Yolk sac transfers the nutrients from uterine glandular secretion or maternal blood. Following implantation and establishment of the chorio-allantoic placenta, there is a transition to haemotrophic nutrition with exchange between maternal and fetal circulations.

Tissue Nutrition during Post-Natal Life

Just after birth baby gets nutrition from *Stanya* (mother milk) which is *Updhatu* of *Rasa Dhatu*. And later on, *Aahar* (food), *Aahar Rasa* (nutrient pool) continuously circulating and nourishes the body. When nutrients reach into tissue through their respective *Srotas,* nutrients are taken up by the action of *Dhatvagni* and get converted into tissue from or utilized for cellular functioning. *Dosha* is formed during the phase of both, digestion and metabolism i.e., *Avasthapaka* and *Vipaka*. The *Dosha* produced at the time of *Avasthapaka* are *Mala Roopi* [Ch.chi. 15/9-11], while produced during the *Vipaka* can be considered as *Dhatu Roopi.* The *Malarupi Dosha, Aahar Mala* and *Dhatu Mala* get nurture by the *Kitta* (metabolic waste products) portion of *Aahar Rasa* [*Ch.Su.* 28/4 and *Ch.Chi.* 15/18].

Dhatu Poshan Nyaya

i. ***Ksheera Dadhi Nyaya* (Law of Total Transformation)-** According to this law as the milk entirely convert into curd, curd into butter milk, buttermilk into butter, butter into *Ghrita* (clear butter) and *Ghrita* lastly into *Ghritamand*. In the same way *Rasa Dhatu* coverts entirely into *Rakta, Rakta* into *Mamsa* and so on *Shukra*, is responsible for causing progeny. Therefore, this law is also known as *Karma Parinama Paksha Nyaya*. As the proceeding *Dhatu* transforms completely into the succeeding *Dhatu*, hence named as *Sarvatma Parinama Paksha Nyaya.*

As per *Lok Purusha Samya Siddhanta*-

Substance	**Dhatu**
Ksheera (milk)	*Rasa*
Dadhi (curd)	*Rakta*
Takra (butter milk)	*Mamsa*
Navneet (butter)	*Meda*
Ghrita (ghee)	*Asthi*
Ghritamand (supernatant of ghee)	*Majja*
	Shukra- Sarva Dhatu Sara (most *Shudh* part)

Time taken for the conversion from initial *Rasa Dhatu* to the last *Shukra Dhatu* is and days as per *Acharaya Charaka* and 30 days as per *Acharaya Sushruta*.

ii. *Kedari-Kulya Nyaya* (Law of Transportation)

According to this *Nyaya*-

Kedar	**Field under irrigation**	***Dhatu***
Kulya	Canal that helps to irrigate fields	*Srotas*
Jal	Water/Nutritional pools	*Ahara Rasa*

Water is supplied to the field by canals. Water that is flowing in the canal is first supplied to the nearest field, after irrigating the requisite amount of water to the field, it flows to the next field and so on. The first field absorbs the necessary part and rest moves into the field. This *Nyaya* shows the sequence and time taken for the replacement of seven *Dhatus*.

Nourishing fluid or the *Ahara Rasa* replenishes *Rasa Dhatu* in the starting. Whatever substance is necessary for its nourishment are absorbed are taken up by *Rasavaha Srotas* where *Rasa-Dhatawagni* work on it and forms *Rasa Dhatu*. *Rasa* replenishes the next *Dhatu*. The whole process of transmission from *Rasa* to *Shukra Dhatu* is completed in seven days.

iii. *Khale-Kapota Nyaya* (Law of Selectivity)

There are two types of *Dhatu* – 1. *Asthayi/ Poshaka Dhatu* which are *Rasa* and *Rakta* 2. *Sthayi Dhatu* (Stable tissue)- rest all *Dhatus*.

Here, *Khala* or field grains are heaped after cutting the crop and *Kapota* or pigeons are the *Poshaka Dhatu*. The pigeons come from different directions and distance to collect the paddy and then fly away to their respective places where they live. Time of returning may vary depending upon distance and direction they have to travel.

As per the law-

Ahara Rasa	Paddy field
Sthayi Dhatu	Nests
Poshaka Dhatu	Pigeons
Dhatuvaha Srotas	Travelling routes of the pigeons
Rasa-Prasarana	Flying force of the pigeons i.e., *Vyana Vata*

As the pigeons move towards their nests i.e., they are attracted by their respective places/nests. The *Sthayi Dhatu* (Stable tissue) attracts their necessary nutrients from the *Ahara Rasa* through their specific *Dhatuvaha Srotas* and nourishes them.

Acharaya Sushruta mentioned that the *Rasa Dhatu* is transporting nutrients to stable *Dhatu* and it stays each of the six *Dhatus* for the time space of 3015 *Kala*. *Rasa Dhatu* takes five days so 3015 *Kala* contribute to each *Dhatu* space. So, as per this essence part took one month to form all *Dhatus*.

Stem Cell Theory

Stem cell is a cell that can replicate itself and differentiate into many cell types. These cells are broadly categories according to the source of stem cells and their differentiation potential.

1. Based on sources

a. Embryonic stem cells: Retrieved from human embryos that are 4-7 days old after fertilization. Embryonic stem cells have special properties like self-renewal, structural repair, growth and rapid cell division.

b. Fetal Stem cells: Stem cells that are extracted from a fetus using fetal blood, bone marrow or tissue such as liver and kidneys after the 8th week of gestation. Fetal stem cells have better intrinsic engraftment, greater multipotency and lower immunogenicity.

c. Adult Stem cells/somatic stem cell: These are the living undifferentiated cells found in differentiated tissues that can renew themselves or can replenish dead or damaged tissue. Somatic refers to non-reproductive cells in the body. ASCc generate cells to replace the diseased or ruptured cells. These cells are found throughout in lifetime in tissues such as the umbilical cord, placenta, bone marrow, muscle, brain, fat, tissue, skin, gut etc.

Types of ASCs

Skin stem cells

Epithelial stem cells

Neural Stem Cells

Mesenchymal Stem Cells

Hematopoietic Stem Cells

d. Umbilical Cord Stem Cells: Retrieved from the umbilical cord blood and placenta of a new born. Shorted hematopoietic stem cells which are used to treat numerous genetic diseases, cancer or inherited disorders.

2. Based on Differentiation Potential

a. Totipotent Stem Cells: Generate all the cell in the organism, zygote or fertilized egg is the best example as it can grow into any cell type, including the placental cell.

b. **Pluripotent Stem cells:** Just prior to implantation in the uterus, when blastocyst formed has inner cell mass and tropho-ectoderm cells. Tropho-ectoderm contribute to the placenta formation while inner cell mass has embryonic stem cells (ESCs). ESCs are pluripotent and give rise to 3 germ layers- ectoderm, endoderm and mesoderm but are unable to generate extra-embryonic tissue i.e., placenta. Adult stem cells could be reprogrammed to mimic the qualities of embryonic stem cells, in the form of Induced pluripotent stem cells (iPSCs). They can develop into more than 200 cell types.

c. Multipotent Stem Cells: Generate only a limited number of cell types based the origin of tissue. They are not pluripotent because they lost the ability to become cells of all three germ layers and present in almost all the tissues.

e.g- Hematopoietic stem cell- give rise to different type of blood cells

Mesenchymal stem cell- give rise to fat, bone, muscle and cartilage

Neural stem cell- give rise to neurons, oligodendrites and astrocytes

d. Oligopotent Stem Cells: Generate few cell types which are closely related- myeloid stem cells

e. Unipotent stem Cells: Generate one cell type- epidermal stem cells, muscle stem cells

DISCUSSION

Dhatu Poshan Nyaya means tissue nutrition and differentiation. Seven *Dhatus* formation starts in the *Garbha* (embryonic stage) but their nutrition and maintenance continued throughout the life.

Differentiation of tissue depends upon the type of stem cells present in the growing fetus at different stage. *Ksheer Dadhi Nyaya* stated that there is complete conversion or total transformation of one type of cell to another cell type. The initial molecule loses its form to transform into another form. According to this law *Dhatu* transcript, translation and transformation takes place within specific period. Like pluripotent stem cell or extra-embryonic (placental) stem cells, these cells are acquired after birth, they are not immortal but have a high level of cell division. These cells after sequential differentiation turn into specific type of cell forming different tissues during the embryogenesis and their nourishment thereafter. This theory suggests that there is a common parent cell of all forming element.

Kedari Kulya Nyaya can be compared to multipotent stem cells or oligopotent stem cells which are of various types depending upon the location, they take up certain nutrient essential for their growth like Hematopoietic stem cell which is a multipotent stem cells give rise to different type of stem cells like myeloid stem cell and lymphoid stem cell which are oligopotent in nature. There is a sequential formation of WBC, RBC and platelets from myeloid stem cell.

Khale Kapot Nyaya can be compared to unipotent stem cells. Every *Dhatu* gets nourished independently from the *Ahara Rasa*. These cells can produce only one cell type and have property of self-renewal that separates them from non-stem cells like epidermal stem cell and spermatogonial stem cells. Like this *Nyaya* states the possibility of nutrition of *Shukra* directly from milk due to *Shukra Poshak Amsha* as per *Guna Samanya (Samanya Vishesh Siddhanta)*. This maxim refers to the selectivity of the cells for uptake of nutrients.

Nyaya's	**Modern Theory**	**Explanation**
Kshira Dadhi Nyaya	Pluripotent stem cell or extra-embryonic stem cell	Theory that explains the total transformation
Kedari Kulya Nyaya	Multipotent stem cell or Oligopotent Stem cell	Theory that explains sequential differentiation
Khale Kapot Nyaya	Unipotent Stem cell	Theory that explains selectivity

CONCLUSION

Nyaya is the laws that explains the idea of nourishment and differentiation sequencing in between *Dhatus* by help of different channels and also not one *Nyaya* is capable to prove the idea according to current scenario, that's why we take all *Nyaya* simultaneously.

Tissue nutrition and differentiation is said to be continuous process, which established just after the conception and remains throughout the life. But the stages of tissues differentiation are not same in different stage of development.

On the basis of above discussion, it is summarized that Ayurveda has discussed a broad spectrum on tissue nutrition and differentiation. The various theories based on tissue nutrition and differentiation in Ayurveda, are do resembles with the today's scenario. The theory of tissue formation and differentiation, during early gestational stage cells are totipotent stem cells and pluripotent stem cells which converts totally into endoderm, mesoderm and ectoderm. This suggests that it follows *Kshira Dadhi Nyaya* (law of complete transformation).

As in *Kedari Kulya Nyaya* water moves sequentially from one canal to the other. Like multipotent stem cell or oligopotent stem cell sequentially differentiate into a particular type of cell and also maintain their self-renewal property. Different types of stem cells from different structures of blood. Example hematopoietic stem cell form into myeloid and lymphoid progenitor cells which further differentiate into different blood cells and immunogenic cells.

As in *Khale Kapot Nyaya* (the law of selectivity), the pigeons move in specific direction to reach their respective nests. The unipotent stem cells have extremely limited differentiation potential and can only develop into a single specialized cell type. Generally, they are associated with the specific regeneration of a type of tissue or organ. Example germ cells (ovary in females and sperm in males), these cells can only differentiate into oocyte spermatocytes, which are very specific and unipotent differentiation.

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