

A CRITICAL APPRAISAL OF RAKTOTPATTI IN THE LIGHT OF HEMATOPOIESIS

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ABSTRACT

To keep up with ever changing, ever growing field of research in modern medical science, the Ayurvedic concepts need to be analyzed and updated. Updating is better effected by critical comparison of Ayurveda concepts with that of modern medical science. Hence literary research gains importance in Ayurveda. *Dhatus* are the basic constituents of human body. *Raktadhatu* is a liquid tissue performing the functions like *jeevana*, *varnaprasada*, *mamsapushti* etc. *Raktotpatti* is a complex procedure. The diseases of blood and faulty hematopoiesis are on the rise. For Ayurvedists to tackle these, a sound understanding of hematopoiesis becomes essential. Therefore the present article throws light on *Raktotpatti* in comparison with hematopoiesis.

Key words: *Rakta*, *Raktotpatti*, Hematopoiesis, Erythropoiesis, *Rasadhatu*, *Ranjaka Pitta*, *Raktadhara Kala*, *RaktavahaSrotas*

RELEVANCE OF PRESENT STUDY

The research is basically classified as pure and applied¹. The applied researches are meant cater the needs of society. The fruitful outcome of applied research depends and demands a sound platform of conceptual study which is the core of pure research.

Ayurvedic researches undertaken during the last 50 years have not been very rewarding except for the extremely useful exercise of literary research, which has at least made a few of the classical *Ayurvedic* texts accessible to contemporary readers and researchers². Similarly a number of literary researches published in recent years have helped create a conceptual interface between Ayurveda and modern science.

The *Ayurvedic* practitioners of modern days can be categorized as 1) those that follow traditional materials methods for diagnosis and treatment and 2) those using

modern materials and methods for diagnosis then implementing *Ayurvedic* treatment, closely abiding the principles of Ayurveda. The physicians belonging to second category need the *Ayurvedic* concepts to be updated in relevance with modern developments. And even the people belonging to first category, for most the orientalist though reiterate that conceptual buildup of Ayurveda and modern science are entirely different, yet they don't oppose the comparison between two similar phenomena in different fields. It is further pointed out that the structural analysis of any phenomenon in particular, gains considerably from comparison with different structure.³

Blood is one among the vital anatomical structure in human body. The vital parts demand more as regards their understanding because the diseases caused to them or by them affect badly.

Diseases like anemia, thalassemia, sickle cell anemia and diseases of faulty hemato- poiesis like leukemia and other hemoglo- binopathies are in want of better therapeu- tic measures. For Ayurvedists to tackle these, the understanding of hematopoiesis in the light of modern science from an Ayurvedic perspective is essential. Hence a need was felt to critically study and analyze the *raktotpatti* in the light of mod- ern science concepts of blood formation thereby provide a firm footing for applied clinical studies on hematology.

METHODOLOGY

Since the present study was a literary re- search, compilation of all the available lit- erature on *Rakta* with special reference to *Raktotpatti* from all available sources was done. Factors that determine *Raktotpatti* were also studied and gathered. Gathered data was analyzed to mitigate the conflicts in textual references. This was followed by collection of information regarding blood and its formation. Thereafter critically each point were analyzed and interpreted.

DISCUSSION

The term *Raktotpatti* talks about the *utpatti* of *Rakta*. The word *utpatti* has various synonyms as *janana*, *janma*, *ud- bhava*, *sansara*, *jati*, *prabhava*, *sambhava* etc. By and large all give the same mean- ing of origin and formation. According to *yaska*⁴, all the structures of the human body represent themselves in six stages viz *Jayate*(formation), *asti* (existence), *viparinamate* (transformation), *vardhate* (growth), *apakasheeyate* (decrease) and *vinashyate* (destruction) which are further simplified and accepted in three forms as *utpatti* (formation, origin), *sthiti* (exist- ence) and *laya* (distruction).

The cause for origin of anything can be traced from philosophical background of *samhitas*. This is briefed in the context of

karyakaranavada. The *Paramanuvada* of *vaisheshikas*, as interpreted by *Achar- yaCharaka* tells that human body is com- posed of *paramanus*⁵. These are innumera- ble, minute and imperceptible to the naked eyes. Conjugation of which lead to organ- ogenesis and cause for both conjugation and separation are *vayu* and *karma swabhava*. Of six *karanas* documented in *Sushruasamhita*, the organogenesis is at- tributed to *swabhava*⁶. The remaining are *ishwara*, *kala*, *niyati*, *parinama* and *yadruchcha*. Here a mention of *satkarya- vada* is also necessary as the formation depends on the ingredients.

In relation to human body, the term *utpatti* can have two meanings.

1. The formation, prior to existence i.e. First time formation.
2. The continuous formation to combat the depletion of *dhatu*s as *sharira* (*shir- yateanen iti*) is always undergoing disintegration and requires replenish- ment (*cheeyate aannadibhi iti*) all the time. Both aspects of formation fall in the purview of present work.

There may appear a confusion regarding the second interpretation as whether it is *utpatti* (formation) or *poshana* (nourish- ment). The formation and destruction are continuous process. Hence the formation and nourishment have no factual differ- ence as the *Raktotpatti/ poshana* is also a relentless process.

The *Samhitas* generally appraise of *Raktotpatti* as 'the *rasa* enters *yakrit* and *pliha* get stained red to be termed as *Rak- ta*⁷. *Chakrapani* quoted of *sthayi* and *poshakadhatu*, which are applicable to *rak- ta* also. The *asthayi* or *poshakaraktadhatu* is the product of digestion whereas the *sthayirakta* is formed by *raktagnivyapara*. The sites of this transformation are *yakrit* and *pliha*. The *Asthayidhatu* represents the

parinamaapadyamanadhatu i.e. the *dhatu* in the state of transformation, carried to *yakrit* and *pliha*.

There is controversy regarding the *raktagnivyaparaas* whether it acts on *poshakaraktadhatu* or *rasa dhatu*. To answer this question, the help of *dhatu-poshananyayas* can be taken. The transformation theory of *ksheeradadhi nyaya*⁸ is strongly supportive of *rasadhatu* being transformed into *rakta*. This is true in respect of embryonic tissue formation. Before the formation of *rakta* only *rasa* pervades all over the body and produces *rakta*. *Kedarikulyanyayata* talks about the formation/ nourishment only when the vasculature is complete, Hence *raktasadharmiamsha*, which is often referred to as *poshakaraktadhatu* is acted upon by *raktagni*, helping *raktotpatti*.

The four methods of *dhatuposhana* can be simplified as 1) Conventional method and 2) Direct method. The Conventional method of formation explains the succeeding *dhatu* formation from preceding *dhatu* i.e. *Rasa torakta*, then *mamsa*, *meda* etc, whereas the second method is supported by reference like *rasamrasena*, *lohitamlohitena* etc. The *rakta* of animals contain enormous *raktasadharmiamsha* required for *raktotpatti* hence majority of requirements of *rakta* formation are met with the utility of *rakta*.

RAKTOTPATTI VIS-À-VIS HEMATOPOIESIS

Blood cell formation is known as hematopoiesis or hemopoiesis [hemato=blood, poiesis= to make]. Despite the extreme structural and functional differences in blood cells, all are the progeny of pluripotent hematopoietic stem cell (PHSC). Hence the process by which the hematopoietic stem cell gives rise to various cellular components of blood is termed hema-

topoiesis⁹. Hematopoiesis therefore involves the differentiation of PHSC into multiple mature blood cell types.

Rasadraktamprajayate¹⁰: All the authorities of Ayurveda have proposed that *rakta* is formed from *rasa*. Though there are authors like Sharangdhara who hold that both *rasa dhatu* and *ahara rasa* are same, the *dhatu rasa* is different from *ahara rasa*, which is supported by statements of Charaka like “*pushyantitu ahararasadrasaraktata*¹¹.....” Thus in this context *rasa* implies *dhatu*.

Blood and lymph are the only two structures that circulate communicating to every cell in the human body, transporting all the requirements of cell metabolism and carrying away the metabolic wastes. Hence an inference would be all requirements of the hematopoietic tissue are provided by blood and lymph, where the blood plasma represents *rasa dhatu* and for most, the formed elements (blood cells) do not carry anything other oxygen. Therefore the *rasadhatu* help the formation of blood, as it transfers dietary requirements, the various the growth factors¹² including cytokines, lymphokines like thrombopoietin¹³, erythropoietin (EPO)¹⁴, to hemopoietic tissue. They even carry the PHSC cells to the environment of bone marrow where hemopoiesis takes place. The growth factors are the regulatory proteins helping in cell multiplication and differentiation. Thrombopoietin and erythropoietin are the hormones secreted for the release of thrombocytes and erythrocytes in circulating blood. The *rasa dhatu*, in human body represents also *twak* (supported by concept of *twaksara* as *rasasara*). The *twak* is outermost covering. In the embryological study, there are three germinal layers ectoderm, endoderm and mesoderm of yolk sac, giving rise to respective organs. The outer-

most layer is ectoderm, which produces skin, nervous tissue, adrenals cortex, adenohypophysis and salivary glands. The primary ectoderm contains the first hematopoietic stem cells and endothelial cells. These cells migrate to the extra embryonic mesoderm, which forms the outer layer of yolk sac wall. This is the major site of embryonic hematopoiesis, where the blood is first formed¹⁵. Hence if the outermost layer i.e. *Twak* can be viewed as outermost layer of embryo i.e. Ectoderm, the support to *rasadraktamprajayate* stands justified.

Pushyanti Tu Ahararasadrasarakta: In the view of charaka, as clarified by chakrapani the nourishment of *sthayirasadidhatu* is done by *Ahararasa* the essence of *jataragnipaka*. It has already been stated that there exists no factual difference between nourishment and formation of *raktadhatu*. The major factors determining the hematopoiesis is the dietary constituents. The dietary requirements of hematopoiesis chiefly include Iron, Vitamin B12, Folic acid, Copper, Cobalt, Vitamin C, Peridoxine, Pantothenic acid etc. An ideal diet/food principally contains all these in crude form and refinement is the subject of digestion. This refined bio-absorbable form is subjected to various bio-chemical activities, so that it becomes useful for hematopoiesis.

Dhatavo-hi-dhatvahara: Ayurveda says that *rasa* forms *rakta*, *rakta* forms *mamsa* etc. That is to say that precursor *dhatu* is the *ahara* for the next *dhatu*. The term *dhatu* as *ahara* in *raktotpatti* can have two meanings. 1) the precursor *rasa dhatu* and 2) the *ahara*, the principle *dhatu* nourishing all *dhatu*s. The *dhatutva* of *ahara* is supported by enumeration of *dhatu*s by Bhavaprakasha in the context of *srotas* as *mana*, *anna*, *pana*, *dosha*, *dhatu*, *mala*; *upadhatu* etc. are all the *dhatu*s undergo-

ing transformation. The *rasa dhatuasahara* for *rakta* substantiated in the discussion on *rasadrasaraktamprajayate* and the *ahara* as *dhatu* for *raktotpatti* is clarified in the context of *PushyantiTuAhararasadrasarakta*.

Dhatuposhanakrama in hematopoiesis:

The theories of transformation (*Ksheeradadhi*) transportation (*Kedarikulya*) and selectivity (*Khalekapota*) influence the hematopoiesis. The requirements for hematopoiesis, in particular the dietary are subjected to transformation by the process of digestion. At the tissue level this is the function of various enzymes. The transformed material needs to be transported to the hematopoietic organs (Bone marrow, liver, spleen etc) which are affected by *kedarakulyanyaya*. The hematopoietic organs are highly specific and take only the absolutely essential factors from blood pool for the hematopoiesis. The selectivity is representative of *khalekapota* theory.

Another implication of these can be, the *ksheeradadhinyaya* exhibits the embryonic hematopoiesis, where the maternal *rasa* produces *rakta*. This is supported as blood formation commences on 17th day and Vasculature develops from 18th gestational day¹⁶. Hence *kedarikulyanyaya* represents the transportation when vasculature is complete.

Agni in hematopoiesis: *Yakrit* and *plihais* the site of formation of *rakta*. The formation of *rakta* involves two distinct steps.

- ✓ The action of *Raktadhatvagni* helping *raktautpatti* and,
- ✓ The *Ranjaka pitta* imparting typical red colour.

In the hematopoiesis the formation of cellular structure in particular RBC is distinct from formation of Hemoglobin.

The *raktadhatvagnivyapara* is indicative of various changes taking place in the

hematopoiesis. The *raktagni* can be correlated with various factors of metabolism that determine hematopoiesis. The factors principally include hematopoietic growth factors (HGF). The HGFs are the regulatory proteins that are both stimulatory and inhibitory. As of today more than 50 proteins are identified¹⁷. These include the growth factors like c-kit ligand, Il-1, 3, 6, 11, thrombopoietin.

Ranjaka pitta in hematopoiesis: The substance which imparts red color to blood is *Ranjaka pitta*. The red color of blood is attributed to Hemoglobin (Hb) present in RBCs. Hb is a red pigment of blood, containing 96% globin bound to 4% of Iron. According to Sushruta, *ranjaka pitta* is located in *Yakrit* and *Pliha*. The Iron in human body (200-500mg) is stored as Ferritin and hemosiderin. 30% of which is in liver, 30% in RBM and rest in spleen and muscle. This suggests that Sushruta's *ranjaka pitta* may well represent the iron in Ferritin and hemosiderin form present in human body.

Vagbhata has identified *ranjaka pitta* in *amashaya*. The principal dietary constituent for formation and maturation of RBCs in vitamin-B12 Vit-B12 requires, for absorption, the intrinsic factor of castle (CIF), which is secreted by parietal cells of stomach¹⁸. The CIF is a glycoprotein that combines with vit-B12 to prevent its digestion by pancreatic juice, so that vit-B12 is absorbed in the terminal ileum. Vit-B12 then is absorbed and stored in liver. Therefore the CIF may well represent vagbhata's *ranjaka pitta*.

Yakrit and Pliha as organs of Hematopoiesis: Ayurveda says that *rakta* is formed in *Yakrit* and *pliha*. In the fetal hematopoiesis the principal organ of blood formation is in liver, from the 5th week of gestation¹⁹. The liver has the precursor of

myelomonocytic cell differentiation produces only red cells. Liver also is a producer of various HGFs. Recently detected HGF²⁰ (Hepatocyte growth factor) produced from liver parenchyma is in extensive research work to analyze hematopoiesis. Spleen is also a hematopoietic organ, both in intra-uterine and extra-uterine life. In the fetus the hematopoiesis in spleen begins in 6th week as the hematopoietic nests migrate from liver, and continues up to 14th week. After which the spleen becomes a lymphoid tissue producing only lymphocytes.

Saraktameda is the *meda* present in small bones. Though the hematopoietic function of *saraktameda* is not mentioned in Ayurveda, yet it appears that the *saraktamedais* RBM (Red bone marrow)

Raktavaha srotas²¹ in Hematopoiesis: *Srotas* are the channels that carry to and from the body cell/tissues. The *Raktavahasrotas* is indicative of transporting the *Raktadhatu* during transformation that is *asthayiraktadhatu*. The *mula* (root) of this *srotas* are *yakrit* and *pliha*. From the *mula*, transformation takes place. This implies that the various products required for hematopoiesis (viz, Fe, vitamin-B12, foliate etc) are transported from liver and spleen, to the hematopoietic organs for hematopoiesis. According to Ayurveda the organs for hematopoiesis are liver and spleen, hence the *Raktavahasrotas* are blood vessels that enter and leave the liver and spleen.

Raktadharakala in Hematopoiesis: *Kala* is a membrane like structure in between the tissues and receptacles²². The primary receptacles (abode) of *rakta* are they *yakrit*, *pliha* and *sira*. The internal lining of these forms the *Raktadharakala*. Therefore the definition of the term *kala* and functions ascribed resemble the protective epithelial

tissue, thus the *Raktadharakala* shows similarity with endothelial layer of blood vessels, capillaries, sinusoids of liver, spleen and marrow (*Saraktamedas*).

The endothelial lining is functionally denoted as reticulo-endothelial system (RES), which is also known as monocyte-macrophage system (MMS) and mononuclear phagocytic system (MPS). This system contains two types of cells. 1) Monocytes in blood and RBM 2) Macrophages in tissues eg: spleen, RBM (called as reticulum cells) and liver (kupfer cells), lung, peritoneum, brain²³. The macrophages can be fixed or wandering. This system in RBM provides adhesive framework on which the developing cells are bound, and produces some hematopoietic growth factors. The other functions are phagocytosis, **Table 1 showing stages of RBC maturation in comparison with Hareeta's opinion.**

Stage	Features	Varna	Appearance
Pronormoblast	Lacks Hb	<i>Shweta</i>	White
Early Normoblast	Lacks Hb, Dense Nucleus/Chromatin	<i>Kapota</i>	Grey
Intermediate Normoblast	Hb Starts Entering, Cell Nucleus Present, Polychromic Cytoplasm	<i>Harita</i>	? Pale Red
Late Normoblast	Hb Increases Nucleus Removed	<i>Haridra</i>	Yellowish
Reticulocyte	Redness Increases	<i>Padmakimshuha</i>	Lotus Red
Erythrocyte	Red	<i>Alaktaka</i>	Red

Time required for Erythropoiesis: In accordance with hareeta it is 7 days, supported by chatterjee's statement that it takes 7 days' time to pass from stage of Pronormoblast to Reticulocyte and another two days for maturation of Erythrocyte and the Reticulocyte are in circulation.²⁵

CONCLUSION

Raktotpatti is one among the complex physiological processes taking place in the body. The *ahara/ahara rasa* provide

scavenging of RBCs and assisting the lymphocyte mediated immunity.

The *raktadharakala* (RES) system of liver and spleen, destruct the senile RBCs causing hypoxia. Hypoxia causes EPO release from kidneys, leading to erythropoiesis. Hence the *raktadharakala* of *yakrit* and *pliha* stimulate *raktotpatti*.

Hareeta's stages of Erythropoiesis

Hareeta has quoted that in *raktotpatti*, the change of color takes place in a particular sequence i.e. *Shweta* to *kapotathen* to *harita* followed by *haridra*, *padmakimshuka* and lastly *alaktaka*²⁴. There appears a striking resemblance of these with the stages of erythropoiesis i.e. Pronormoblast, early normoblast, intermediate normoblast, late normoblast, reticulocyte and erythrocyte. (Table 1)

all the dietary requirements that are transported to the abode of *raktadharakala* by *rasadhatu* through *raktavahasrotas* for *raktotpatti*. *Raktotpatti* demands normalcy of *pachakagni*, *rasagni*, *raktagni*, and *dranjaka pitta*. Advances in field of hematology have put forth the clearer picture of complex hematopoiesis. As regards the *Raktotpatti* vis-a-vis hematopoiesis, the hematopoietic organs can be paralleled to *Yakrit* and *pliha*, which are hematopoietic in fetal

life, retaining their capacity to do so in emergency condition, various HGFs can be paralleled to the concept of *Dhatwagni*, the *Ranjaka pitta* can be compared with the iron and Intrinsic factor of Castle. With these parallels Ayurveda practitioners can try address diseases of blood as well as diseases of faulty hematopoiesis.

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