RELEVANCE OF PRESENT STUDY
The research is basically classified as pure and applied\(^1\). The applied researches are meant to 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 researchers\(^2\). 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 orientalists 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 anatomo-physiological 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 hematopoiesis like leukemia and other hemoglobinopathies are in want of better therapeutic measures. For Ayurvedists to tackle these, the understanding of heamatopoiesis 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 modern science concepts of blood formation thereby provide a firm footing for applied clinical studies on hematology.

**METHODOLOGY**

Since the present study was a literary research, compilation of all the available literature 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 uttpatti of Rakta. The word uttpatti has various synonyms as janana, janma, udbhava, sansara, jati, prabhava, sambhava etc. By and large all give the same meaning of origin and formation. According to yaska\(^4\), all the structures of the human body represent themselves in six stages viz Jayate(formulation), asti (existence), viparinamate (transformation), vardhate (growth), apakasheeyate (decrease) and vinashhyate (destruction) which are further simplified and accepted in three forms as uttpatti (formation, origin), sthiti (existence) and laya (destruction).

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 AcharyaCharaka tells that human body is composed of paramanas\(^5\).These are innumerable, minute and imperceptible to the naked eyes. Conjugation of which lead to organogenesis and cause for both conjugation and separation are vayu and karma swabhava. Of six karanas documented in Sushruasamhita, the organogenesis is attributed to swabhava\(^6\).The remaining are ishwara, kala, niyati, parinama and yadruchcha. Here a mention of satkaryavada is also necessary as the formation depends on the ingredients.

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

1. The formation, prior to existence i.e.
   - First time formation.
2. The continuous formation to combat the depletion of dhatus as sharira (shiryaate anen iti) is always undergoing disintegration and requires replenishment (cheeyeate 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 uttpatti (formation) or poshana (nourishment). The formation and destruction are continuous process. Hence the formation and nourishment have no factual difference 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 Rakta\(^7\).Chakrapani quoted of sthaya and poshakadhatu, which are applicable to raktaloe. 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. TheAsthayidhatu represents the
parinamaapadyamanadhatu i.e. the dhatu in the state of transformation, carried to yakrit and pliha.

There is controversy regarding the raktagniyaparas whether it acts on poshakaraktadhatu or rasa dhatu. To answer this question, the help of dhatuposhananyayas can be taken. The transformation theory of ksheeradadi nyaya is strongly supportive of rasadhatu being transformed into rakta. This is true in respect of embryonic tissue formation. Before the formation of rakaonly rasa pervades all over the body and produces raka. Kedarikulyanyaya talks about the formation/nourishment only when the vascularlature 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, lohitamlohit etc. The raka of animals contain enormous raktasadharmiamsha required for raktotpatti hence majority of requirements of raktaperformation are met with the utility of raka.

**RAKTOTPATTI VIS-À-VIS HEMATOPOIESIS**

Blood cell formation is known as hemato poiesis 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- topoiesis. Hematopoiesis therefore involves the differentiation of PHSC into multiple mature blood cell types.

**Rasadraktamprajayate**: 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 ahararasadrasaraka” Thus in this context rasa implies dhatu.

Blood and lymph are the only two are 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 growth factors including cyto kines, lymphokines like thrombopoietin, erythropoietin (EPO), to hemopoietic tissue. They even carry the PHSCells 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 outer most 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 formed. 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 sthayirasadidhatus is done by Ahararasa the essence of jataragnipaka. It has already been stated that there exists no factual difference between nourishment and formation of rakta dhatu. 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 raktoptatti can have two meanings. 1) the precursor rasa dhatu and 2) theahara, the principle dhatu nourishing all dhattus. The dhatutva of aharais supported by enumeration of dhatus by Bhavaprakasha in the context of srotas as mana, anna, pana, dosha, dhatu, mala; upadhatu etc. are all the dhattus undergoing transformation. The rasa dhatuasahar-afor rakta substantiated in the discussion on rasadrasarakta and the ahara as dhatu for raktoptatti 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 maternalrasa produces rakta. This is supported as blood formation commences on 17th day and Vasculature develops from 18th gestational day. Hence kedarakulyanyaya 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. 1) The action of Raktadhatvagni helping raktautpatti and, 2) 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 raktadhatvagnivivyapara 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 identified\textsuperscript{17}. 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 Fe\textsubscript{r}-ritin and hemosiderin.\textsuperscript{30} 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 stomach\textsuperscript{18}. 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 5\textsuperscript{th} week of gestation\textsuperscript{19}. The liver has the precursor of myelomonocytic cell differentiation produces only red cells. Liver also is a producer of various HGFs. Recently detected HGF\textsuperscript{20} (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 6\textsuperscript{th} week as the hematopoietic nests migrate from liver, and continues up to 14\textsuperscript{th} 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 srotas**\textsuperscript{21} in Hematopoiesis: Srotas are the channels that carry to and from the body cell/tissues. The *Raktavahasrotas* is indicative of transporting the Raktadhatus 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.

**Raktadharakaka in Hematopoiesis:** *Kala* is a membrane like structure in between the tissues and receptacles\textsuperscript{22}. The primary receptacles (abode) of raktare are theyakrit, pliha and sir. The internal lining of these forms the Raktadharakaka. Therefore the definition of the term *kala* and functions ascribed resemble the protective epithelial
tissue, thus the Raktadhara\(\text{a}\)kala shows similarity with endothelial layer of blood vessels, capillaries, sinusoids of liver, spleen and marrow (\textit{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, brain\(^{23}\). 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, scavenging of RBCs and assisting the lymphocyte mediated immunity. The raktadhara\(\text{a}\)kala (RES) system of liver and spleen, destruct the senile RBCs causing hypoxia. Hypoxia causes EPO release from kidneys, leading to erythropoiesis. Hence the raktadhara\(\text{a}\)kala of yakrit and pliha stimulate raktopatti.

**Hareeta's stages of Erythropoiesis**

Hareeta has quoted that in raktopatti, the change of color takes place in a particular sequence i.e. Shweta to kapotathen to harita followed by haridra, padmakimshuha 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)

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

**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**

Raktopatti is one among the complex physiological processes taking place in the body. The \textit{ahara/ahara rasa} provide all the dietary requirements that are transported to the abode of raktadhara\(\text{a}\)kala by rasadhatuthrough rakta\textit{vahasrotas} forraktopatti. Raktopatti demands normalcy of pachakagni, rasagni, raktagni, andranjaka pitta. Advances in field of hematology have put forth the clearer picture of complex hematopoiesis. As regards the Raktopatti 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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