LITERARY REVIEW:

Since the study comprises the details of *Kala, Raktadhara Kala* and the test drug *Gunja* etc, hence the Literary Review is being done in following headings,

1. Literary Review about the word Kala.
2. Literary Review about Raktadhara Kala.
3. Structure of Raktadhara Kala.
4. Clinical Importance of Raktadhara Kala.
5. Development of Mesoderm.
7. Structure of Spleen.
10. Literary review of Gunja, the test drug.
1. **Literary Review about the word Kala.**

   The knowledge of bodily structure is invariably essential for its benefit i.e., for keeping the body healthy. A physician unless & until knows all the intricate secrets of this body, he cannot comprehend the factors that are beneficial for this body.

   *Acharya Sushruta* pioneer of *Rachana Shareera* presented the science of *Kala Shareera* in the chapter “*Garbhavyakarana nama Shareera*” under which he tried to emphasize the concept of *Kala* along with fundamental science.

   While composing the Anatomical and Physiological Sciences *Ayurvedic Acharya’s* thought much for the basic constituents of the body (*Dhatu*) and their substratum (*Ashaya*). While considering upon the *Ashaya* they had also thought of the linings making internal walls of the *Ashaya*, designating them as *Kala*. They presented it in a very silent way.

**ETYMOLOGY OF KALA**

The word *Kala* has been derived from the root

कल-गति संख्या ने, माती - means movements,

संख्यान- means counting. It belongs to the चुगबिना.

According to Panini Dhatupata page No – 50 and Dhatu Sl. No. 1865.

कल्लगति इति कला-means which moves and counts is known as Kala.

Derivation is as follows हुकला + गुच्छ + अच् = कला.

The Sutra निधिमहिष्ठार्द्धिक्यो त्वागिन्य च: Panini Astadhya – 3-1-134.
Here the suffix हृ अव्व is added with root in the sense of कर्ता means agent (subject) which moves ahead itself and which enable other things to counts i.e why it is called as Kala.

_Gati_ is one of the main characteristic features of the living beings. Without _Gati_ there is no meaning for the life, life started from single cell. This single cell is also capable of performing all kind of movements. But in multi cellular animals movements i.e the actions are increased in organization, such as growth, nourishment, multiplication, blood circulation, response to the external stimuli etc. By knowing all these things clearly we can say the functions or movements of the living beings can proportionally categorized into three types:

1. **Molar Motion**- One part of the body is able to exert influence on another one. By this the body, by its part as a whole becomes a source of relating mass motions.

2. **Metabolism**- By this material composition of the body is maintained by the balance of the process of waste on one hand and those of assimilation on the other hand.

3. **The Process of Reproduction**- It is nothing but development of a part with the power of developing and existing as independently.

Development and growth of the human being starts since from the combination of _Shukra_ and _Shonita_. The fertile ovum converted into zygote. After entry of a sperm into the oocyte some changes takes place:

The fertilized ovum begins to divide into several cells i.e cleavage. As cleavage proceeds the two celled ovum became 16 cells ovum and looks like as much every and called as the morula.

Further the development continues in all the organs and systems. At last when the development completes, it is called as _Sharira_,

This body is able to perform all kind of molar motions, metabolism, assimilation etc. after delivery _Sharir_ attain child hood, adult age and old age, these are also movement of the _Sharir_. The word _Sharir_ is derived from the root शियति अनेत्र इति शरिरम्.

The structure that is going to be decaying in every minute is called as _Sharir_. In this structure the catabolism (destructive process) and anabolism (constructive) process
are going on simultaneously. To perform all these kinds of functions this physical body is having the structures like skin, Kala, Peshi, Snayu, Sira, Dhamani etc to know all these structures of body and to protect the body and to treat the disease, we have to study the body in detail.

i.e.-

शरीरविच्छ: शरीरोपकारधामिप्यते ।
ज्ञातवाहिः शरीरतत्वं शरीरोपकारकरेशु आवेषु ज्ञाजमुतप्यते ।
तरमाच्छ शरीरविच्छं प्रशंसान्ति कुशला:— ्च. शा. ६

The Ayurved is the science of life in which two main principles are explained

-स्वस्थ्यस्य स्वास्थ्य रक्षण
-आतुर्वस्य विकार प्रशमनः

To fulfill these two principles we must have the normal structural and functional knowledge of the body. By dissecting the dead body physician can have occult knowledge of the body.

So Susruta in his Samhita Sharir Sthana 6th chapter explained the method of dissection and study of Sharir.

While dissecting the dead body we encounter with some smooth silky cloth like layer, in between tissue and organs, which separate them and help in the individualization of the tissue organs and systems of the body and make them to count in number like Sapthadhatu, Sapthaashaya, three Malasa, is called as Kala.

Without Kala the body parts and organs are not separated and counted. So this important structure of the body separating the body organs fixing them in their place and preventing the friction between them while functioning, since from the embryonic stage by forming three germ layers that is why Susutra presented to this in Sharir Sthana 4th Chapter as follows.
Kala are seven in number and behaving like a land marks, in the individualization of Dhatus and Ashayas and makes them to count in number. Again Susruta in Sharir Sthana 5th chapter has described.

This counting of body organs E.g Twacha are seven, Kalas are seven, Ashaya are seven etc is possible because of Kala in between body structures.

HISTORICAL BACKGROUND OF KALA

The word Kala has been used in various senses in General Sanskrit, Vedic and Ayurvedic literature. In Ayurveda, which is the science of life while dealing with Sharir Rachana and Sharirakriyavijna the word, Kala has been used in different context with different meaning. However in anatomy it is admissible only in one meaning. The following quotations of ancient lexicographers will show the various meanings of Kala in common parlance.

In Amarakosh:

1. कलातु चोड़ो भाग - The sixteenth part of the moon.
2. कीर्ततु ताः (काष्ठ) कला - Increase on capital invested (interest on profit)
3. कलाशिल्पे कालमेघः - Measure of time,<sup>7</sup> कालमान्
In Medinikosh:

कला स्यादंश्च चलनां विभाग विभागमात्रके।
योडशांशे च तन्त्रस्य कलना– कालमान्योः॥

1. The sixty four fine arts.
2. Collation – कलना

In Hemachandrakosha,

कला स्यादंश्च–शिल्प्योः। अ चीत्तील्लेप – अंशमान्म

In Amarakosh: (Vyakhyasudhakhya commentary)

तालेपु च गुरुः कलना। -the long strokes in music - तालमाण्म

These are the seven meanings ascribed to the word Kala in literary field.

Kalas in Vedic literature:

The term Kala has been used very frequently in almost all the Vedas.

In Rig-Veda also the term Kala is mentioned like this,

यथा कलां यथा शणं यथा अर्ण स्तनयामसि।
एवा दुष्टवर्धं सर्वमासं सं ज्ञातस्यनेहंसो व अतयं: सुअतयो व अतयं॥ 8/47/11

Its literary reveals that “As we collect the utmost debt, even the 8th and 16th part, so unto Aptya we transfer together all the evil dreams”. 
In \textit{Atharvana Veda} also we came across with the terms \textit{Kala}. There it has been said like this.

\begin{quote}
यथा कलां यथा शरं यत्नं संख्ययती।
एवा हस्तपृः सर्व द्विपेत सं नयामसि 6/46/3
\end{quote}

Means-As a sixteenth as an eighth as a (whole) debt they bring together. So do we bring together all evil dreaming for him who hates us. In another context in same \textit{Veda} it has been stated like this\textsuperscript{10}.

In the same \textit{Atharvana-Veda} there is mention of the word \textit{Kala} and stated liked this:

\begin{quote}
सं राजानो अमुः समृणान्यमुः सं कुष्ठा अमुः सं कला अमुः।
समर्मामु यदु दुष्कार्यं निर्दिष्टो दुष्कार्यं सुवाम् || 19/57/2
\end{quote}

Means – Kings have gathered debts have gathered, \textit{Kushtas} have gathered, sixteenth have gathered; all evil dreaming that is in us-Let us impel away evil-dreaming to him that hates us.

\textbf{Kalas in Upanishats:}

1. In \textit{Brihadaranyaka-Upanishada}: In \textit{Brihadaranyaka-Upanishada} there is mention of word \textit{Kala}

\begin{quote}
स एष संवल्सरः प्रजापतिः प्रदशाकलतरस्य राज्य एव।
पञ्चदश कलाध्ववार्ष्य णोडशी कला || 1/5/14
\end{quote}

Means-\textit{Prajapati} is the year\textsuperscript{11}, and he consists of sixteen \textit{Kalas} (digits) the night indeed are his fifteen \textit{Kala} (digit), the fixed point his sixteenth \textit{Kala}. 
2. In *Prashnopanishad* - In *Prashnopanishad* we came across with the word *Kala* while answering to a question it has been told like this:

इत्यादि शरीरे सौम्य सा पुरुषे यस्मिनेतरः कला: प्रभवलिति ||

Means—that person is here within the body he in whom these sixteen parts (*Kala*) arises\(^{12}\).

in another context in same *Upanishad*, it has been stated that,

अरा इव शतांशि कला यस्मिनप्रतिपूर्वः: ||

tे वेत्य पुरुष वेद यथा मा वो मृत्युः परिवर्त्या इति || 6/6

Means—The person who is to be known, he in whom these *Kalas* (parts) rests like spokes in the nave of a wheel, you know him, lost death should heart you.

3. In *Mandookopanishad*: In *Mundakopanishad* there is a mention of term ‘*Kala*’, while explaining about the *moksha*\(^{13}\) (emancipation) like this was:

जगतः कला: फल्वदश प्रतिष्ठा देवाश्च सर्वं प्रतिविश्वासु।
कर्माणि विज्ञानमयश्च आत्मा परेर्वेय सर्वं एकीभवन्ति || 3/2/7

Their fifteen parts (*Kala*) enter into their elements, their *Devas* (the senses) into their corresponding *Devas*. Their deeds and their self with all his knowledge became all one in the highest imperishable.

Thus in *Vedas, Upanishadas* the word ‘*Kala*’ has been used mainly in four senses:

1) Fractions  2) Component Parts

3) Qualities  4) Part of time.
Kala in Puranas:

1. In Vishnupurana:

In Vishnupurana also the term Kala has been used in the sense as time\textsuperscript{14} i.e.

\begin{verbatim}
निमेखी मातुरी तयों मात्रा मात्राप्रमाणतः
तः पञ्चदशमिः काष्ठा त्रिशताकष्ठा कला रम्यतः
नाइका तु प्रमाणे रा कला दशा पञ्च च
6/3/6 and 7
\end{verbatim}

Means Matra is Nimesh of a person. Fifteen such Nimesha make one Kashtha and Thirty Kashtha make one Kala and fifteen Kalas make one Nadika.

2. In Agnipurana:

In Agnipuran (68) also we find the description about Kala. All the seven Kala are mentioned similar to that of Sushruta\textsuperscript{15}.

Kala in Ramayana and Mahabharat:

Ramayana and Mahabharat are holy treatise of Hindu culture they deal with the history, religion, culture and Marshal art of ancient India. Since there are not concerned with the subject of Hindu medicine as such while going through the review of literature in these texts nothing found specific related with that of the biological and medical aspect of Kala.
DEFINITION OF KALA:

Kalas are the marginal lines between the Dhatus and Ashayas. Different physical components of the body e.g. Rakta, Mamsa, Mala, etc can be kept individually which are seven in number. Means they cannot be mixed with each other. This individualization of physical components of the body is possible only because of the presence of Kala in between them. Skin is the organ, which covers the body components externally. ‘Kala’ is the structure, which covers the body components internally is called as ‘Kala’. By the virtue of Kala only all the body components are kept separately.

Kalas are the layer like structure situated in the body. They are the structures which separate the Dhatus from the Ashayas.

- The things formed from the connective tissue-fasciculus i.e Snayuvat.
- The membranous- layer like structure which is fibrous, serous or mucous due to the effect of Kapha. The definition of the Kala and functions ascribed about seven Kalas in the Ayurvedic scripts resemble to the protective or epithelial tissue.
- The Gunas – Qualities
- शरीर के विभिन्न घटक -Parts of the body- as Sushruta explained in the Uttara Tantra those Shodasha Kalas are - Seven Dhatukalas, three Dosh Kalas, three Aharkalas (gas, solid, liquid) three Mala Kalas (considerably)

- चाराकी पादं बोधक कलं - In Charaka, while explaining the Chikitsa Chatuspada Adhyaya he used the word Kala in the sense of Gunavachi.
Kala is explained while studying the cadaver from external to internal\textsuperscript{19}-…

That’s why he found Mamsa after removing the skin so mentioned the first Mamsadhara Kala i.e. प्रथम मांसधराणम्, after dissecting this Mamsadhatu he found the network of Sira and Dhamani which are related to the blood circulation and mentioned as the Raktadhara is the second Kala

i.e. द्वितिय स्रकधराणम्.

Then he found the Snigdha Bhaga which is attached to the Mamsadhatu i.e Meda so he mentioned the Medhodhara Kala is third one.

i.e. तृतियमेडधराणम्.

After that he found the Asthi that is hard and strong not suitable thing with the meaning of “Kala” -membranous smooth, jelly part of the body. So he omitted this part and not mentioned the Asthidhara Kala.

Next he found the body joint with synovial membrane, bearing the synovial fluid in synovial cavity. That is why he mentioned fourth as the Shleshmadhara Kala.

i.e. चतुर्थ श्लेष्मधराणम्.

Then he opened the abdomen and found the large intestine. The place from which Purishotpatti takes place, called Purishadhara Kala

i.e. fifth one पंचमी पुरीशधराणम्.
But *Swedodhara Kala* and *Mutradhara Kala* have not been mentioned. *Sweda* is not got as absorbed from the sweat duct and skin.

But in *Annavaha srotus* there is a same kind of absorption all along its length, till the expulsion of *Pureesha*. Means most useful part of the body that is why he mentioned the only *Purishdhara Kala*.

After that he found the *Agyashaya, Yakrit, Pleeha* and mentioned sixth *Kala* is as *Pittadhara Kala* in relation to that

i.e. षड्ठी वित्तधाराम् and

Lastly he mentioned *Shukradhara Kala* which is spread all over the body as सातमि शुक्रधाराम।

**Textual Compilation of KALA SHARIR.**

1. **Kala in Charaka Samhita**:  

    Maharshi Charaka does not use *Kala*’ in the sense of body organs or parts. He has used the word *Kala* only to mean the qualities, while explaining the *Maha Chatushpada Adhya* in *Sutrasthana*°.

    चतुष्पादं षोडशकलां भेषजमिती | - च.० 10/3
    
    *Charaka* says therapeutics has four legs. Again each leg is having four-four qualities total sixteen qualities. Such therapeutics has the capacity to cure the disease and give the previous health to the diseased person.

2. **Kala in Sushruta Samhita**:  

    In *Sustrasthana* of Sushruta Samhita ‘*Kala*’ word has been used in the sense of time°.

    त्रिशद् काष्ठ: कला, विशेषतिकलो मुहूर्तः | यु.० 6/5

“Confirmation of Anatomical structure of Raktadhara Kala in animal model”  

Page 17
Means-Thirty Kashthas makes one Kala and Twenty Kalas make one Muhurta. According to Sushruta one Kastha is equal to fifteen Akshinimesha. One Akshinimesha means, the time taken to articulating any one of the short vowel example such as ‘A’ etc. Further Sushruta in 14th chapter Sutrasthan i.e., Shonitavarnaneeya Adhyaya he used the word Kala as the meaning of period (time) by quoting this Shloka.

Rasa Dhatu stays 2015 Kala in one Dhatu and lastly became Shukra in males and Arthava in females in one month i.e, 18090 Kala. Again in Uttar Tantra he used the word Kala in the sense of sub-strata of the body i.e.

Dalhana in his commentary commented upon this verse in this way.

Those sixteen Kalas are Panchamaha Bhootas (Five elementary principles) and eleven Indriyas (five jnanendriya, five karmendriya and one ubhayatmaka manas). Dalhana again used the word Kala in the sense of body parts- Head, Neck, Upper limbs, Lower limbs, Scapular and lumbar region, Abdomen - eight parts and Chinn, Nose, Lips, Vanshkana, Thumb fingers, Heel, Gulfa - eight parts. Totally they are sixteen in numbers that is why Purush is the combination of sixteen components (Kalas)- Purush: पूर्व:।
Means pleasure, displeasure, desire, aversion, effort, inspiration, expiration, blinking of eye lids, intelligence, mind intension, analysis and discrimination, memory or recollecting capacity, knowledge, attempt, perception of sense are the sixteen qualities (Kala) of living beings. These features generally called as Atma Lingas or Atma Lakshnas. These Shodasha Gunas of Atma are interpreted as Shodash Kala by, Dr. Ramasundar Rao in this book ‘Shareer Kriyavijnan’

Further he explained, if new born baby bears all these qualities that baby is considered as Shodasha Kala Paripurna that is full-fledged living being.

All these properties are seen only in lived persons. In dead persons these qualities are not seen.

How our outer body surface is covered and protected by the skin, in the same way the body internal Angapratyang as Eg - Sapthadhatus, Saptashayas etc., are covered and protected by the thin membranous lining called by the name Kala. Sushruta again in Kalpasthan mentioned the word Kala while explaining the “Sarpadansha Chikitsam chapter like this.

After the explanations of Vishavega Sankhya are seven, further he is justifying why Vishavegas are only seven. Because Dhatus are also seven and the Kalas which are located in between them are also seven so vishavegas are also seven in number. Further he used the word Kala in same chapter while explaining how the visha under goes Vegantar.
The time taken by the Visha to cross the one Kala with help of Vata is called Vegantar. And in Sharirasthana, Sharira Sankhya Vyakaran Adhyaya 5th chapter after considering Angas, then Pratyanga Sankhya has been explained in this way.

Further in same chapter he explained the Sankhya of Kala as seven in number.

Sushruta in Sutrasthana Vrinasrava Vijnaney Adhyan that is 22nd chapter while dealing with Amashayagat (Kostha) Vrina he used the word Amashayakalagat Vrina. From these Vrina there is a oozing of blood, urine, feces, pus and plasma.

Again in Chikitsa Sthana he used the word Kala while explaining the Sadhyovrina Chikista like this.

If colon is protruded from the abdomen and is to be pushed back to its place with the help of finger.

Sushruta has described Kalas in the Sharira Sthana with anatomical sense while dealing with Garbha Vyakarana Adhyaya (Embryology) he defined Kala like this,
According to Sushruta the Kalas are seven in number and are situated in the interior of the receptacle for Dhatu and act as separator for Dhatu (content) from their Ashayas (container) 31.

यथा हि सारः काष्ठे धियमानेषु द्वश्यते ।
तथा धातुहि मांसेषु धियमानेषु द्वश्यते ॥

Sushruta says Kala can be seen in the cadaver after removing the skin and Mamsa. How the Saar Bhaga of the timber is seen after removing its bark 32.

र्नामुमिच विपक्षान्त संततांशं जरायुणा ।
श्लेष्मणा वेद्दितांशं पि कलाभागांर्तु तान विदु ॥

In Sushruta says these Kalas are such parts of the body as are interspersed with fibrous tissue (snayu) pervaded by thin membranous structure (serous) and enveloped by Shleshma (mucus) 33.

3. Kala in Kashyapa Samhita:

In Kashyapa Samhita the word Kala is used in the sense of काल 34(time, seasons)

तस: कलसमुहः काल द्विविधमकल्पतं शुभम् च ......... काश. -1

In Kashyapa Samhita Sharira Sthana first chapter at beginning while explaining about the Ritu, he quoted above Shloka, which means the god Brahma created the काल (time seasons) by the combination of group of Kala’s – कलासमुहः कालम् which is of two types:

1) शुभ - auspicious
2) अशुभ -inauspicious.
4. **Kala in Asthang Sangraha** – Vagbhata –I,

He has used the word *Kala* in the sense of body organ\(^{35}\).

\[\text{वर्तु धात्वाश्यान्तरेणु बलेदे वर्तिष्टे स वयधात्वमृत्तिग्रिजः} \]
\[\text{रणायुश्लेष्मजरमायुष्मः काठ इव सारो धातुसारस्मृते} \]
\[\text{रसश्चोपत्पत्वात् कलान्त्रः। तात् धात्वाश्यान्तरमयः। सस कला।} \]

अ.सं.शा. 5/19

It is like the heartwood of plants, the residual part of the essential *Dhatu* and is termed *Kala*. On account of its less important function or structure it is also called by the synonyms *Alpatwa*’ i.e, smallness.

After which he has explained individual *Kalas*, which are considered afterwards.

5. **Kala in Vagbhata-II** While describing in *Sharira Sthana* the word *Kala* in is *Angavibhaga Shariram* quoted the *Shloka* like this.

\[\text{धात्वाश्यान्तरेणि विषः स्वरूपमृत्तिग्रिजः} \]
\[\text{श्लेष्मजरमायुष्मः कलाख्यः काठस्मृते। तत:। सस:। आ.ह.शा.3/9,10} \]

The moisture (*Kleda*) present inside the *Dhatu* (tissues) i.e. contents and *Ashayas* (organs) i.e. containers, is processed by their own *Agni* (heat of each *Dhatu* and *Ashayas*) become converted into membranous structures called by the name ‘*Kala*’ just as essence gets formed in the trees and found after removing the bark. These are smeared with *Shleshsma* (*Kapha*), *Snayu* (tendinous waxy material) or *Apara* (chorion). These are seven in number\(^{36}\).

The *Kleda* of *Dhatu* which is present in the *Dhatus* is get heated by the body heat in combination with *Snayus*, *Shlesma* and *Jarayu* to form *Kala*. Because it is small in amount so defined as *Kala*. To denote this he used the word *Alpa*. The word *Alpa* also meaning the microscopic. But in general ‘*Alpa*’ or *swalpa* is used in *Sanskrit* script to denote the small in amount or size but not as microscopic. To clarify this he is given the example of heartwood, which is composed after the removing of bark. So the root principle is removing the successive layers of the cadaver may see the *Dhatus* of the body.
6. Kala in Bhavaprakasha:

In Bhavaprakash Nighantu, Bhavamishra explained about the Kala and use in the sense of body parts\(^\text{37}\). In Garbha Prakaran he is quoted like this

अमालखयाद्धः पक्राशयाद्धं वृत्तं, याकला।

श्राहणो नामिका सैव कस्तिक पावकशय।

भा. पु-खंडा 3/214

There is a lining membrane just below the Amashaya and above the Pakwashaya, is called by the name ‘Grihini’ the same organ is also called as Pachamanashaya, it indicate the Pittadhara Kala. Further in same chapter he is explained the Kala in detail:

र्नामुषमश प्रतिहार्यानु संबत्ताशं जरायुणा

श्लेष्माण बेटिततांश्चापि कला भाषांतु ताल्लितः॥

धातवशाल्यात्रे धातोध: वलेद स्वाधिमिधितः

deहोषमातिमिश्रस सा कलेष्मिधियते॥

भा.पु-खंडा 3/219, 220

Bhavamishra explained the Kala Swaroop like this covering of Snayu, spread like Jarayu and looks like as if streaked in mucus part of the Dhatwashaya which is moist in nature and became transformed to membranous like structure by the effect of Dheha - ushma, such parts of the body are called by the name Kalas.

Further Bhavamishra explained the seven Kala in order like this

आध-भारस्थारित्रा प्रेक्षा द्वितिया स्त्रीधारिणी।

मेथोधारातीत्या तु च तुर्थे श्लेष्मधारिणी।

फलवसी तु मलं धते चंदी पित्तधारा मता।

रेतोधारा सास्मी स्वाधिमिधी सता कलाः स्मृता॥ - भा.पू-खण्डा 3/221, 222

He explains the serial order of seven Kalas as Mamsadhara, Raktadhara, Medodhara, Shleshmadhara, Maladhara, Pittadhara and seventh is Retodhara Kala.\(^\text{38}\)
7. Kala in Sharangadhara Samhita:

*Sharangadhara* also used the word *Kala* in the sense of parts of the body, and told they are seven in number\(^\text{39}\).

Further he is naming all the *Kalas* in order.

First *Kala* is ‘Mamsadhara Kala’ which holds the *Mamsadhatu*. Second *Kala* is ‘Raktadhara Kala’ which hold the *Rakta*. Third one is ‘Medhodhara Kala’ which bears the *Medha Dhatu*. Fourth layer which is situated in between *Yakrit* and *Pleeha*. But its name is not mentioned. Fifth one is situated in between two *Antra* and holds the *Purish* called by the name *Purishadhara Kala*. Sixth *Kala* bears the *Agni* so called by the name ‘Agni Kala’. Seventh one is named as ‘Retodhara Kala’ and holds the *Shukradhatu*. These are the seven ‘Kalas’ explained by *Sharangadhara*.

8. Kala in Adhamalla Commentary on Sharangadhar Samhita:

*Adhamalla* while commenting upon the word *Kala* described in *Sharangadhara Samhita* says that the moisture of the *Dhatus* (tissues) undergoes transformation by the effect of *Agni* (their *dhatwagni*) of the body and forms the membranous structures known by the terms *Kala*. The quotation as follows,

\[
\text{धात्वाश्यान्तरस्तर्यं खलेदश्चत्वधिष्ठितम्} \\
\text{देहोप्रथमा विपक्षे च: सा कलेत्यमिदितवते} \quad \text{॥ शा.सं. 5/1}
\]
9. *Kala in Dalhan and others:*

In his commentary stated that ‘*Kala*’s are covers the different *Dhatus* inaccessible and may limits it in to be understood by its virtue. Again he used ‘Avyatka’ to denote *Swaroop*. Its literal meaning is invisible but here its meaning is inferiorly situated not seen on living body, only seen while studying the cadaver.

Taking some of these sutras in account Pandit Gangadhar Shastri Joshi commenting in his book “*Ayurvediya Sharira*” that *Kala* are must be exceedingly minute and visible because *Charaka* has also stated that organs of the body of minute invisible innumerable magnificently differentiated. But the basis selected for this conclusion. The *Charaka sutra* is not applied for numerable organ, which are included in the *Sankhya Sharira*. In *Charaka Kalas* are not directly mentioned.

In modern era the contribution of *Mahamahopadhyaya Kaviraj Gananath Sen Saraswati* by the title of संज्ञापन्यास - विमर्श: a book published from *Krishnadas Academy, Varanasi* is quotable, which has given much light in the area of *Kala*. 
3. **LITERARY REVIEW ABOUT RAKTADHARA KALA.**

a. **DEVELOPMENT OF RAKTADHARA KALA:**

In our *Samhitas*, there is no exact reference’s regarding the development of *Raktadhara Kala*, so we can assume that:

**In embryonic period – Jarayu Santata:**

“ज्यायुतूल्याकाशां चेत वेषिता: प्राणिनो ज्यात्मने: कलावेषको अधि तंद्रेव ॥

दृष्टिज्ञः सु.श.४१८

*Acharya Dalhana* commenting on *Swaroopa* of *Kala* described that, it is like *jarayurulbaka*, which covers the embryo during intrauterine life.

**According to Sir Monier Williams:**

ज्यायु – means withering, dying away, outer skin of embryo or amnion and chorion.

उल्बक – means, the membrane enveloping the embryo.

वेषिता – means, enveloped, bound round, wrapped up, enclosed, surrounded etc. So by above reference we can assume that, structure of *Raktadhara Kala* is resembling or similar the structure of *Jarayu* i.e. the membrane enveloping the embryo or Amnion and Chorion of embryo during the intrauterine life.
b. **STHANA OF RAKTADHARA KALA:**

*Raktadhara Kala* is one among the *Sapta Kalas*, in the sequence wise as a second *Kala*. It is a membranous structure holding the *Rakta*, present inside the *Mamsa* in generally and specially present in *Sira, Yakrit and Pleeha*. In this quotation *Sushruta* has given more importance to *Sira, Yakrit and Pleeha* for presence of *Raktadhara Kala* only to denote some special function of this *Kala* in these organs.

*Vagbhata* -I in *Shareerasthana* described the same i.e. *Raktadhara Kala* is present inside the *Mamsa* in generally and especially in *Sira, Yakrit and Pleeha*.

c. **STRUCTURE OF RAKTADHARA KALA:**

*In Mamsaabhyantara*

According to Sir Monier Williams:

*Mamsa* – fleshy part, *Abhyantara* — interior, being inside of, included in.

Both *Sushruta* and *Vagbhata*-1 mentioned that *Raktadhara Kala* is generally present in *Mamsaabhyantara*. While describing *Mamsadhara Kala* both Acharyas mentioned that inside the *Mamsa, Sira, Dhamani, Srotases* are spread. By this we can understand that within the muscle we will get *Rakta* which circulating in the tubular structure i.e. *sira* and *dhamani*.

In modern science we can interpret that blood vessels are spread inside the muscle. And these blood vessels are lined by membranous structure.
Structure of **Sira**:

**Definition:**

*Siras* are the channel or tubular structures where the function of *sarana* (continuous motion) takes place in all over the body. *Chakrapani* states that *siras* communicate to various (peripheral) parts of the body. Kaviraja Gangadhara said, *Rasa, Rakta* and other *Dhatus* are carried through these *siras*.

*Siras* are found all over the body in the form of a network. They travel to various parts of the body. Hence definition सरणाद indicates the spreading out of *siras* all over the body as *Cakrapani* mentions सरणाद देशान्तरणम.

Structure of **Dhamani**:

**Derivation of word Dhamani:**

The structure which having the pulsation, inspiration, filling with, and nourishes the body is called as *Dhamani*.

**Definition:**

*Dhamanis* are the structures in which pulsations are present. Etymological derivation of *dhamani* is that structure which fills, nourishes the body and allows all the normal functions in the body.

The term *Dhamani* is derived from the root “dhmana” meaning to be filled with substance like *rasa* etc. hence these structures are always found to pulsate in the body.

**Swaroopa:**

According to Gananathsena – Blood is flows from heart through these *Dhamanis*. Its walls are thick and strong and pure blood is flowing in this *Dhamanis*. Kaviraj Gangadhara in his *Jalpakalpataru tika* described, *Dhamanis* are different from *siras* because of pulsations, and within the *Dhamani* we find holes.

**According to Chakrapanidatta:**

Because of pulsations which happen in them due to filling up with *Rasadi bhavapadartha*, they are called as *Dhamani*. 
Moola sthana:

Acahraya Susruta has described Nabhi as the Moolastana of Dhamani. And move upwards, downwards and obliquely in the body. They are 24 in number.

Utpatti and Nirmana Ghataka:

Acharya Sushruta included Dhamani in Pitruja Bhava. He has told the origin of Dhamani from the group of Panchamahabhuta. And he has said in Sharirastana that the ushma of pitta mixes with vayu and then through Dharana Prakriya (tearing apart process), Srotas is formed. Dhamani is also Avakashayukta (spacious) like srotas. So we can conclude the Utpatti of Dhamani takes place in the same way as that of Srotas. Just as by the nature, vacant spaces are present in the flower stalk and tuber of the lotus plant; similarly, vacant spaces are present in the Dhamani also, through which Rasa (nutrient tissue) gets nourished during spreading to the entire body.

Dhamani - Sira – Srotas:

From above description we can understand that all avakashayukta(spacious) channels can be included in the terminologies of Dhamani, Sira, and Srotas.

Reason for similarities:

1. परस्परस्थितिक्षण : nearness
2. परस्परस्थितिक्षण : all have similar functions
3. सौक्ष्म्यच च : all are Sookshma in nature.
Reason for differences:

1. व्यवस्थानान्वलनः: differences in Akruti, Lakshana, and chinha.
2. मूलस्त्रियमात्र: difference in moolastana
3. कर्मचारीशोषणः: functions special to each.
4. आगमात्माः: the description of each at different places in Sushruta
   Samhita.

So, by above description about Dhamani- Sira- Srotas we can interpret that the transport of Poashaka Bhava-Padartha occurs through Srotas and that of Poshya Bhava-Padarth flows through sira and Dhamani. From this it is clear that is a bigger and much larger entity than Sira. In this way, considering Srotas as a different entity than Sira.

Structure of Yakrit and Pleeha

Sushruta in the Shrirastana described Yakrit, Pleeha and Raktavaha dhamanis are the principle organs of Raktavaha sroats.43

In Charaka samhita there is no reference of Kala in relation to body structure but in the Vimanasthana described Yakrit and Pleeha are moolasthana of Raktavaha srotas.

Rakta is circulating in the whole body through Raktavaha srotas and is protected and sustained by Raktadhara Kala. And it is especially present in Yakrit and Pleeha indicating some special function of Raktadhara Kala in these organs. Sushruta in Sutrastana mentioned that Yakrit and Pleeha as the Ashaya of Rakta. Raktashaya is the place where Rakta resides. It is termed as Raktadhara in Vachaspatyam and Shabdhalakpadruma. Even Vagbhata termed Yakrit and Pleeha as Raktadhara.
All Acharyas opined Yakrit and Pleeha as moola of Raktavaha Srotas. But Acharya Sharangadharra considers only Pleeha as moola of Raktavaha Srotas, where as Yakrit as the sthana of Ranjaka pitta as well as Shonita. Sushruta in Sutrasthana mentioned Ranjaka pitta is located in Yakrit and Pleeha. And these are the moolasthana of Raktadhatus. When Rasa dhatu gets installed in the Yakrit and Pleeha, the Teja (Ranjaka pitta) brings red color to this Rasa is called Rakta. And it circulates in the whole body through the Siras. Being located in Yakrit and Pleeha, Rakta spreads other parts of the body. In the living being channels of circulation of blood are controlled by these organs.

**Formation of Yakrit and Pleeha:**

The Yakrit and Pleeha are formed from Shonita in the Garbha.

**Nirukti and Sthana of Yakrit:**

Kalakhanda is the synonym of Yakrit and it is present on right and lateral side.

**Paryaya:** In Paarishadhyya Shabdhartha Shareera –

कालखण्ड, ज्योतिस्तान, चक्रत्थष्ठ, चक्राल्पिण्ड, रक्ताधार, रक्ताशय, अग्रांस

**Sthana of Pleeha:**

Pleeha is situated below the Heart and to the left.

Sharangadhara mentioned only Yakrit as the Ranjakapitta stana. In formation of Rakta, along with Yakrit, pleeha is considered as Raktashaya, and Raktadhara.
a. FUNCTIONAL ASPECT OF RAKTADHARA KALA:

As Raktadhatu which carries Pranavayu and cells present in Raktadhatu are responsible for jeevanakriya. So by this we can understand that function of Raktadhara Kala is by holding the Rakta it gives protection to Raktadhatu. And also we can understand that life is holed or protected by these Raktadhara Kala, as Sharangadhara mentioned that,

रक्तां जीव इति स्थिति

So we can give more importance to this Kala out of seven Kalas. As these membrane holding the life\(^48\). Sushruta described that if any injury to this membrane in muscle, immediately blood flows out in great quantity, it may leads to death. As Rakta is considered as one of the Pranayatana by both Charaka and Vagbhata.

**Karya of Sira**

By the Siras the entire body is nourished constantly, kept lubricated or moistened to perform actions such as flexion, contraction, extension, dilatation etc, similar to a large field being nourished by small channels of water; their spreading is like the leaves of the trees; Nabhi is their moola and from there, these spreads upwards, downwards, and side wards\(^49\).

**Karya of Dhamani:**

The word Dhamani itself means that, the structure which fills, nourishes the body and allows all the normal functions in the body.
**Karya of Yakrit:**

**Yakrit as a Jyotisthana:**

In Paarishadhya Shabdhartha Sharira described that,

There are two reasons for Garbha vrudhi. One is Rasa which gives nourishment and another one is Vayu helps in cell division and growth. Rasa is entered the Garbha through Nabhi nadi attached to the apara. Vayu is present in the Jyotistana and from there it does its function and Garbha vrudhi occurs. It is very difficult to mention which is the Jyotistana. The Rakta of garbha through Nabhi is directly enters into yakrit from here it is distributed all over the body. From Yakrit collected blood enters into the Hrudaya through adhara mahasira.  

Through the Nabhi, Rakta is directly enters into jyotistana. In Garbha vrudhi instead of presence of Rasa and vata, jyoti itself or due to sthana of Agni it does its important function. Ayurveda consider through this Jyotisthana Garbha vridhhi occurs. Here Jyotisthana is none other than Garbhhasya Yakrit (fetal liver).

d. **APPLIED IMPORTANCE OF RAKTADHARA KALA:**

Both Sushruta and Vagbhata -1 described Raktadhara Kala in traumatological aspect i.e. when muscle get injured immediately blood flows out in great quantity, this indicates injury to Raktadhara Kala. If blood flows out in great quantity, leads to death. As Sharangadhara is mentioned that रक्तधरा काला जीव ड़रति स्तिति  

And also as one of the Pranayatana. So one should protect this Kala especially in Mamsa, Sira, Yakrit and Pleeha.
**Dhamani Pratichaya:**

According to Sir Monier Williams: *Pratichaya* can be split up into two words: *Prati + Chaya* from which the meaning *Prati* means towards or near to, *Chhaya* means shadow or reflection, from this the meaning of *Pratichaya* can be taken as the *sanchaya* (accumulation) in every place (in each Dhamani or at each place in Dhamani).

From the above *sootra*, it is quite clear that *Sanchaya* (accumulation) of *Doshas* always takes place in their specific *sthanas*. But we don’t find *Dhamani* mentioned as a *sthana* of any *Dosha* in the *Samhitas*. But since, *Dhamani* and *Sira* do the transport of *Rasadi Bhavapadartha*, we can assume *Chaya* is the accumulation of these *Bhavapadartha* in them\(^1\). *Chakrapani* has mentioned the meaning of *Pratichhaya* as *Upalepa* and *Upalepa* meanse *Avarana*\(^2\).

In case of *Dhamani*, the meaning of *Mala* can be taken as *Vikrita Bhava padhartha* and so in this context, *Dhamani Pratichaya* will mean the accumulation of *vikruta Rasadi Bhavapadartha* as well as *Avarana* of the same on the inner walls of *Dhamani*\(^3\).

*Charaka Samhita* in *Sutra Sthana* 20th Chapter of 17th *Shloka*, we can find the term ‘*Dhamani pratichyaya*’ which means enlargement of arteries due to accumulation of surplus *kapha* in them. And it is a known fact that *Kapha* and *Meda* properties are similar to each other. Aggravation of former leads to the aggravation of latter and so as in vitiation also. Diseases of *Meda* are otherwise diseases of *Kapha*.

**Granthi:**

*Dhooshita vatadi Doshas* cause *Dushti of Mansa – Rakta – Kapha and Meda Dhatu* which in turn causes the formation of round swelling raised above from the surface of the skin, is known as *Granthi*\(^4\).
Sira Granthi:

In a person who is weak, indulging in more of physical exercises, Vata gets aggravated, invades the network of veins, Squeezes, constricts and dries up and gives rise to an elevated, quick developing and round swelling of the veins known as Sira Granthi. But this cannot be compared with deep vein thrombosis or D.V.T as there is formation of blood clot which looks like Granthi and not the twisting of Dhamani which causes DVT, so DVT called as Siragata Rakta- Granthi.

Sirakoutilya:

The signs and symptoms of Sirakoutilya are similar to that of Siragata Vata. The Shoola and Akunchana causes Siravistruti (engorgement).

Udara Rogas:

According to Sir Monier Williams: Udara means enlargement of the abdomen due to any morbid abdominal affection (as of the liver, spleen)

Pleehodara:

In persons who are habituated to foods which cause burning sensation during digestion, and which produce more moisture in the tissues, then asrik (blood) and Kapha become vitiated greatly, make for enlargement of the Pleeha (spleen) gradually, in the left side of the abdomen especially, and produce Pleehodara (abdominal enlargement due to enlargement of spleen).
Yakrddalyudara:

Enlargement of the Yakrit (liver) on the opposite side (right side) giving rise to enlargement of the abdomen is known as Yakrddalyudara\textsuperscript{58}.

Dakodara:

The person who is undergoing therapies such as drinking fats (oleation), oil enema, emesis, purgation or decoction enema, if he drinks cold water immediately, then its srotas become smeared with fatty materials and give rise to Dakodara. The abdomen is unctuous, big, umbilicus is bulged out, the abdomen resembles a bag filled with water both in movement and sound; this disease is known as Dakodara\textsuperscript{59}. So by above reference we can interpret that in diseases described by our Acharyas like Dhamani Pratichaya, Siragata Rakta Granthi, Sira Koutilya, Pleehodara, Dakodara, etc. may affect the Structure and function of Raktadhra Kala.
MEMBRANOUS STRUCTURES

Membranes are flat sheets of pliable tissue that cover or line a part of the body. The majority of membranes consists of an epithelial layer and an underlying connective tissue layer and is called epithelial membranes. The principal epithelial membranes of the body are mucous membranes, serous membranes, and the cutaneous membrane, or skin. Another type of membrane, a synovial membrane, lines joints and contains connective tissue but no epithelium.

Epithelial Membranes:  

Epithelia may be derived from ectoderm, mesoderm or endoderm although in the past it was thought that true epithelia were only of ectodermal or endodermal origin. Two types of epithelia derived from mesoderm, i.e. the lining of blood and lymphatic vessels and the linings of the serous body cavities, were not considered to be epithelia and were termed endothelium and mesothelium, respectively. By both morphological and functional criteria, such distinction has little practical value; nevertheless, the terms endothelium and mesothelium are still used to describe these types of epithelium.

Simple epithelia:

Simple epithelia are defined as surface epithelia consisting of a single layer of cells. Simple epithelia are almost always found at interfaces involved in selective diffusion, absorption or secretion. They provide little protection against mechanical abrasion and thus are not found on surfaces subject to such stresses. The cells comprising simple epithelia range in shape from extremely flattened to tall columnar, depending on their function.

Eg:- flattened simple epithelia are ideally suited to diffusion and are therefore found in the air sacs of the lung (alveoli), the lining of blood vessels (endothelium) and lining body cavities (mesothelium). All blood vessels are lined with simple squamous epithelium called Endothelium.
Mucous Membranes:

A mucous membrane or mucosa lines a body cavity that opens directly to the exterior. Mucous membranes line the entire digestive, respiratory, and reproductive tracts, and much of the urinary tract. They consist of a lining layer of epithelium and an underlying layer of connective tissue. The connective tissue layer of a mucous membrane is areolar connective tissue and is called the lamina propria, so named because it belongs to the mucous membrane. The lamina propria supports the epithelium, binds it to the underlying structures, allows some flexibility of the membrane, and affords some protection for underlying structures. It also holds blood vessels in place and is the vascular source for the overlying epithelium. Oxygen and nutrients diffuse from the lamina propria to the covering epithelium; carbon dioxide and wastes diffuse in the opposite direction.

Serous membrane:

A serous membrane or serosa lines a body cavity that does not open directly to the exterior (thoracic or abdominal cavities), and it covers the organs that are within the cavity. Serous membranes consist of areolar connective tissue covered by mesothelium (simple squamous epithelium)
Cutaneous Membrane:

The cutaneous membrane or skin covers the entire surface of the body and consists of a superficial portion called the epidermis and a deeper portion called the dermis. The epidermis consists of keratinized stratified squamous epithelium, which protects underlying tissues. The dermis consists of dense irregular connective tissue and areolar connective tissue.

Synovial Membranes:

Synovial membranes line the cavities of freely movable joints (joint cavities). Like serous membranes, synovial membranes line structures that do not open to the exterior. Unlike mucous, serous, and cutaneous membranes, they lack an epithelium and are therefore not epithelial membranes. Synovial membranes are composed of a discontinuous layer of cells called synoviocytes, which are closer to the synovial cavity (space between the bones), and a layer of connective tissue (areolar and adipose) deep to the synoviocytes. Synoviocytes secrete some of the components of synovial fluid.
5. DEVELOPMENT OF MESODERM

Initially the cells of the mesodermal germ layer form a thin sheet of loosely woven tissue on each side of the midline. (Fig.2) By approximately the 17th day, however, cells close to the midline proliferate and form a thickened plate of tissue known as paraxial mesoderm(Fig.2).

Fig. 02. Transverse sections showing development of the Mesodermal germ layer.


More laterally, the mesoderm layer remains thin and is known as the lateral plate. With the appearance and coalescence of intercellular cavities in the lateral plate, this tissue is divided into two layers. (Fig.2) A layer continuous with mesoderm covering the amnion, known as the somatic or parietal mesoderm layer, and a layer continuous with mesoderm covering the yolk sac, known as the splanchnic or visceral mesoderm layer. (Fig 2.C, D)
Together, these layers line a newly formed cavity, the intra embryonic cavity, which is continuous with the extra embryonic cavity on each side of the embryo. Intermediate mesoderm connects paraxial and lateral plate mesoderm. (Fig. 2. B, D).

**Lateral plate mesoderm:**

Lateral plate mesoderm splits into parietal (somatic) and visceral (splanchnic) layers, which line the intra embryonic cavity and surround the organs. (Fig. 2 C, D, & Fig. 3 A). Mesoderm cells of the parietal layer surrounding the intra embryonic cavity form thin membranes, the mesothelial membranes, or serous membranes, which will line the peritoneal, pleural, and pericardial cavities and secrete serous fluid. (Fig. 3 B) Mesoderm cells of the visceral layer form a thin serous membrane around each organ.

![Diagram of embryonic layers](image)

**Fig.03.** A. Transverse section through a 21-day embryo in the region of the mesonephros showing parietal and visceral mesoderm layers. B. Section at the end of the fourth week.
BLOOD AND BLOOD VESSEL FORMATION:

Fig 04. Blood vessels form in two ways: vasculogenesis (top), in which vessels arise from blood islands, and angiogenesis (bottom), in which new vessels sprout from existing ones.

Fig 05. Extraembryonic blood vessel formation in the villi, chorion, connecting stalk, and wall of the yolk sac in a presomite embryo of approximately 19 days.
Formation of Blood Vessels:

Blood vessels form in two ways Vasculogenesis, whereby vessels arise from blood islands (Fig.5) and angiogenesis, which entails sprouting from existing vessels. The first blood islands appear in mesoderm surrounding the wall of the yolk sac at 3 weeks of development and slightly later in lateral plate mesoderm and other regions (Fig.5). These islands arise from mesoderm cells that are induced to form hemangioblasts, a common precursor for vessel and blood cell formation.

Although the first blood cells arise in blood islands in the wall of the yolk sac, this population is transitory. The definitive hematopoietic stem cells are derived from mesoderm surrounding the aorta in a site near the developing mesonephric kidney called the aorta–gonad–mesonephros region (AGM). These cells colonize the liver, which becomes the major hematopoietic organ of the embryo and fetus from approximately the second to seventh months of development. Stem cells from the liver colonize the bone marrow, the definitive blood forming tissue, in the seventh month of gestation, and thereafter, the liver loses its blood forming function.

Molecular regulation of Blood Vessel formation:

Fibroblast growth factor 2 (FGF-2) induces blood island development from competent mesoderm cells that form hemangioblasts. Hemangioblasts are directed to form blood cells and vessels by vascular endothelial growth factor (VEGF), which is secreted by surrounding mesoderm cells. The signal to express VEGF may involve Homeobox protein (HOXB5), which up regulates the VEGF receptor Fetal Liver Kinase 1 (FLK1) (Fig.4).

Hemangioblasts in the center of blood islands form hematopoietic stem cells, the precursors of all blood cells; whereas peripheral hemangioblasts differentiate into angioblasts, the precursors to blood vessels. These angioblasts proliferate and are eventually induced to form endothelial cells by VEGF secreted by surrounding mesoderm cells (Fig.4). This same factor then regulates coalescence of these endothelial cells into the first primitive blood vessels.

Once the process of vasculogenesis establishes a primary vascular bed, which includes the dorsal aorta and cardinal veins, additional vasculogenesis is added by angiogenesis, the
sprouting of new vessels (Fig.4). This process is also mediated by VEGF, which stimulates proliferation of endothelial cells at points where new vessels are to be formed. Maturation and modeling of the vasculature are regulated by other growth factors, including platelet- derived growth factor (PDGF) and transforming growth factor β (TGFβ), until the adult pattern is established. Specification of arteries, veins and the lymphatic system occurs soon after angioblast induction\textsuperscript{62}.

6. ANATOMY OF BLOOD VESSELS:

INTRODUCTION\textsuperscript{63}:

The five main types of blood vessels are arteries, arterioles, capillaries, venules, and veins.

\textbf{Arteries} - Large, elastic arteries leave the heart and divide into medium-sized, muscular arteries that branch out into the various regions of the body. Medium-sized arteries then divide into small arteries.

\textbf{Arterioles} – small arteries in turn divide into still smaller arteries called arterioles.

\textbf{Capillaries} – small arteries enter a tissue, they branch into numerous tiny vessels called capillaries. These having thin walls and allow the exchange of substances between the blood and body tissues.

\textbf{Venules} - Groups of capillaries within a tissue reunite to form small veins called venules.

\textbf{Veins} - Venules in turn merge to form progressively larger blood vessels called veins. Veins are the blood vessels that convey blood from the tissues back to the heart. Arteries and veins are named primarily according to their anatomical position. In functional terms, three main classes of vessel are described: resistance vessels (arteries, but mainly arterioles), exchange vessels (capillaries, sinusoids and small venules) and
capacitance vessels (veins). Structurally, arteries can also be divided into elastic and muscular types.

Arteries may also be subdivided into conducting and distributing, as well as resistance vessels. The large conducting arteries which arise from the heart, together with their main branches, are characterized by the predominantly elastic properties of their walls. Distributing vessels are smaller arteries supplying the individual organs, and their wall is characterized by a well-developed muscular component. Resistance vessels are mainly arterioles. Small and muscular, they provide the main source of the peripheral resistance to blood flow, and they cause a marked drop in the pressure of blood which flows into the capillary beds within tissues.

Capillaries, sinusoids and small (post capillary) venules are collectively termed exchange vessels. Their walls allow exchange between blood and the interstitial tissue fluid which surrounds all cells: this is the essential function of a circulatory system. Arterioles, capillaries and venules constitute the microvascular bed, the structural basis of the microcirculation.

**BASIC STRUCTURE OF BLOOD VESSEL:**

The wall of a blood vessel consists of three layers, or tunics, of different tissues, With the exception of capillaries and venules.

- An inner lining by – epithelial tissue,
- A middle layer by - smooth muscle and elastic connective tissue,
- Outer covering by - connective tissue.

The three structural layers of a generalized blood vessel from innermost to outermost are the tunica interna (intima), tunica media, and tunica externa (adventia).
TUNICA INTIMA (INTERN):  
Word meaning:  
Tunic = garment or coat, interna or intima = innermost.  

- It forms the inner lining of a blood vessel and is in direct contact with the blood as it flows through the lumen, or interior opening, of the vessel.  
- Its main component, the endothelium, lines the entire vascular tree, including the heart, and the lymphatic vessels.  
- Although this layer has multiple parts, these tissue components contribute minimally to the thickness of the vessel wall.
**Endothelium:**

- The innermost layer is called endothelium, which is continuous with the endocardial lining of the heart.
- The endothelium is a thin layer of flattened cells that lines the inner surface of the entire cardiovascular system (heart and blood vessels).

**Sub endothelial layer:**

- Consisting of delicate connective tissue with branched cells lying in the interspaces of the tissues

**Baseline membrane:**

- The second component of the tunica interna is a basement membrane deep to the endothelium.

**Internal elastic lamina:**

- The outermost part of the tunica interna, which forms the boundary between the tunica interna and tunica media, is the internal elastic lamina (lamina - thin plate).
- The internal elastic lamina is a thin sheet of elastic fibers with a variable number of window-like openings that give it the look of Swiss cheese.
TUNICA MEDIA:

Word meaning – media = middle

- It is a muscular and connective tissue layer that displays the greatest variation among the different vessel types.

- In most vessels, it is a relatively thick layer comprising mainly smooth muscle cells and substantial amounts of elastic fibers.

- The primary role of the smooth muscle cells, which extend circularly around the lumen like a ring encircles your finger, is to regulate the diameter of the lumen.

TUNICA EXTERNA:

Word meaning – externa = outermost

- It is the outer covering of blood vessel, consists of elastic and collagen fibers.

ARTERIES:

Word meaning - ar = air, ter = to carry

- Arteries were found empty at death, in ancient times they were thought to contain only air.

- The wall of an artery has the three layers of a typical blood vessel, but has a thick muscular to elastic tunica media.

- Due to their plentiful elastic fibers, arteries normally have high compliance, which means that their walls stretch easily or expand without tearing in response to a small increase in pressure.
ARTERIOLE:

Literally meaning - small arteries.

- Arterioles are abundant microscopic vessels that regulate the flow of blood into the capillary networks of the body tissues.
- The approximately 400 million arterioles have diameters that range in size from 15 micrometers to 300 micrometers.
- The wall thickness of arterioles is one half of the total vessel diameter.
- **Tunica interna**: Arterioles have a thin tunica interna with a thin, fenestrated (with small pores) internal elastic lamina that disappears at the terminal end.
- **Tunica media**: consists of one to two layers of smooth muscle cells having a circular orientation in the vessel wall.

Meta arteriole:

- The terminal end of the arteriole, the region called the Meta arteriole, tapers toward the capillary junction.

At the Meta arteriole–capillary junction, the distal most muscle cell forms the pre capillary sphincter, which monitors the blood flow into the capillary; the other muscle cells in the arteriole regulate the resistance (opposition) to blood flow.

- **Tunica externa**: consists of areolar connective tissue containing abundant unmyelinated sympathetic nerves. This sympathetic nerve supply, along with the actions of local chemical mediators, can alter the diameter of arterioles and thus vary the rate of blood flow and resistance through these vessels.
CAPILLARIES:

Word meaning - (capillus - little hair)

- It is the smallest of blood vessels, have diameters of 5–10 micrometer, and form the U-turns that connect the arterial outflow to the venous return.
- Since red blood cells have a diameter of 8 micrometer, they must often fold on themselves in order to pass single file through the lumens of these vessels.
- Capillaries form an extensive network, approximately 20 billion in number, of short (hundreds of micrometers in length), branched, interconnecting vessels that course among the individual cells of the body.
- This network forms an enormous surface area to make contact with the body cells.

Microcirculation:

- The flow of blood from a meta arteriole through capillaries and into a post capillary venule is called the microcirculation (micro - small) of the body.

Absence of capillaries - In a few tissues, such as all covering and lining epithelia, the cornea and lens of the eye, and cartilage.

Importance of structure of capillaries:

1. The structure of capillaries is well suited to their function as exchange vessels because they lack both a tunica media and a tunica externa.
2. Capillary walls are composed of only a single layer of endothelial cells and a basement membrane, a substance in the blood must pass through just one cell layer to reach the interstitial fluid and tissue cells.
3. Exchange of materials occurs only through the walls of capillaries and the beginning of venules.
4. The walls of arteries, arterioles, most venules, and veins present too thick a barrier.
5. Capillaries form extensive branching networks that increase the surface area available for rapid exchange of materials.

In most tissues, blood flows through only a small part of the capillary network when metabolic needs are low. However, when a tissue is active, such as contracting muscle, the entire capillary network fills with blood.
Capillary bed:

- Throughout the body, capillaries function as part of a capillary bed, a network of 10–100 capillaries that arises from a single meta arteriole.

Fig. 07. Structure showing the Blood flowing through capillary bed.

In most parts of the body, blood can flow through a capillary network from an arteriole into a venule as follows:
1. Capillaries.

- In this route, blood flows from an arteriole into capillaries and then into venules (postcapillary venules).

  **Precapillaries sphincters:** control the flow of blood through the capillaries. When these sphincters are relaxed (open), blood flows into the capillaries; when they contract (close or partially close), blood flow through the capillaries ceases or decreases.

- **Vasomotion:** Typically, blood flows intermittently through capillaries due to alternating contraction and relaxation of the smooth muscle of metarterioles and the precapillary sphincters. This intermittent contraction and relaxation, which may occur 5 to 10 times per minute, is called vasomotion. In part, vasomotion is due to chemicals released by the endothelial cells; nitric oxide is one example. At any given time, blood flows through only about 25% of the capillaries.

2. Thoroughfare channel.

- The proximal end of a metarteriole is surrounded by scattered smooth muscle fibers whose contraction and relaxation help regulate blood flow.

- The distal end of the vessel has no smooth muscle; it resembles a capillary and is called a thoroughfare channel. Such a channel provides a direct route for blood from an arteriole to a venule, thus bypassing capillaries.

**TYPES OF CAPILLARIES:**

The body contains three different types of capillaries: Continuous capillaries, fenestrated capillaries, and sinusoids.
Continuous capillaries:

- Most capillaries are continuous capillaries, in which the plasma membranes of endothelial cells form a continuous tube that is interrupted only by intercellular clefts, gaps between neighboring endothelial cells.

- Continuous capillaries are found in the central nervous system, lungs, skin, muscle tissue, and the skin.

Fenestrated capillaries:

Word meaning - fenestr- window

- Other capillaries of the body are fenestrated capillaries.

- The plasma membranes of the endothelial cells in these capillaries have many fenestration, small pores (holes) ranging from 70 to 100 nm in diameter.

- Fenestrated capillaries are found in the kidneys, villi of the small intestine, choroid plexuses of the ventricles in the brain, ciliary processes of the eyes, and most endocrine glands.
Sinusoids:

Word meaning: sinus – cavity.

- Sinusoids are expanded and are large and irregular in shape.
- Their endothelial cells may have unusually large fenestrations.
- In addition to having an incomplete or absent basement membrane, sinusoids have very large intercellular clefts that allow proteins and in some cases even blood cells to pass from a tissue into the bloodstream.
- For example, newly formed blood cells enter the bloodstream through the sinusoids of red bone marrow.
• In addition, sinusoids contain specialized lining cells that are adapted to the function of the tissue.

• Sinusoids in the liver contain phagocytic cells that remove bacteria and other debris from the blood.

• The spleen, anterior pituitary, and parathyroid and adrenal glands also have sinusoids.

• Usually blood passes from the heart and then in sequence through arteries, arterioles, capillaries, venules, and veins and then back to the heart.

**Portal system:**

• In some parts of the body, however, blood passes from one capillary network into another through a vein called a portal vein. Such a circulation of blood is called a portal system.

• The name of the portal system gives the name of the second capillary location.

• For ex- there are portal systems associated with the liver (hepatic portal circulation) and the pituitary gland (hypophyseal portal system).

**VENULES:**

Word meaning – little vein.

• Venules and veins have thin walls that do not readily maintain their shape.

• Venules drain the capillary blood and begin the return flow of blood back toward the heart.

**Post capillary venules:**

• When two or more capillaries converge, the resulting vessel is larger and is known as a venule (postcapillary venule).

• Venules that initially receive blood from capillaries are called postcapillary venules.

• They are the smallest venules, measuring 10 micrometer to 50 micrometer in diameter, and have loosely organized intercellular junctions (the weakest endothelial contacts encountered along the entire vascular tree) and thus are very porous.

• Function: Significant sites of exchange of nutrients and wastes and white blood cell emigration, and for this reason form part of the microcirculatory exchange unit along with the capillaries.
Muscular venules:

- As the postcapillary venules move away from capillaries, they acquire one or two layers of circularly arranged smooth muscle cells.
- These muscular venules (50 micrometer to 200 micrometer) have thicker walls across which exchanges with the interstitial fluid can no longer occur.
- The thin walls of the postcapillary and muscular venules are the most distensible elements of the vascular system; this allows them to expand and serve as excellent reservoirs for accumulating large volumes of blood.
- Blood volume increases of 360% have been measured in the postcapillary and muscular venules.

VEINS:

- Veins, in general, have very thin walls relative to their total diameter (average thickness is less than one-tenth of the vessel diameter).
- They range in size from 0.5 mm in diameter for small veins to 3 cm in the large superior and inferior venacavae entering the heart.
- Although veins are composed of essentially the same three layers as arteries, the relative thicknesses of the layers are different.
  - **Tunica interna**: of veins is thinner than that of arteries.
  - **Tunica media**: of veins is much thinner than in arteries, with relatively little smooth muscle and elastic fibers.
  - **Tunica externa**: of veins is the thickest layer and consists of collagen and elastic fibers.
- Veins lack the internal or external elastic laminae found in arteries.
- The pumping action of the heart is a major factor in moving venous blood back to the heart. The contraction of skeletal muscles in the lower limbs also helps boost venous return to the heart.
Valves$^{64}$:

- Most veins have valves to prevent reflux of blood.

- A valve is formed by an inward projection of the intima, strengthened by collagen and elastic fibers, and covered by endothelium which differs in orientation on its two surfaces.

- Surfaces facing the vessel wall have transversely arranged endothelial cells, whereas on the luminal surface of the valve, over which the main stream of blood flows, cells are arranged longitudinally in the direction of flow.

- Most commonly two, or occasionally three, valves lie opposite one another, sometimes only one is present. They are found in small veins or where tributaries join larger veins.

- The valves are semi lunar (cusps) and attached by their convex edges to the venous wall. Their concave margins are directed with the flow and lie against the wall as long as flow is towards the heart.

- When blood flow reverses, the valves close and blood fills an expanded region of the wall, a sinus, on the cardiac side of the closed valve. This may give a “knotted” (varicose) appearance to the distended veins, if these have many valves.

**Vascular (venous) sinus**

- It is a vein with a thin endothelial wall that has no smooth muscle to alter its diameter.

- The surrounding dense connective tissue replaces the tunica media and tunica externa in providing support.

- **For ex**: 1. Dural venous sinuses, which are supported by the dura mater, convey deoxygenated blood from the brain to the heart.

  2. A vascular sinus is the coronary sinus of the heart.
BLOOD DISRIBUTION:

- 64% is in systemic veins and venules.
- 13% of the blood volume in Systemic arteries and arterioles
- 7% in systemic capillaries
- 9% in pulmonary blood vessels
- About 7% in heart.

Blood reservoir: systemic veins and venules contain a large percentage of the blood volume; they function as blood reservoirs from which blood can be diverted quickly if the need arises.

BLOOD RESERVOIR FUNCTION OF THE VEINS 65:

- More than 60% of all the blood in the circulatory system is usually in the veins. For this reason and also because the veins are so compliant, it is said that the venous system serves as a blood reservoir for the circulation.

- Indeed, even after as much as 20% of the total blood volume has been lost, the circulatory system often functions almost normally because of this variable reservoir function of the veins.

SPECIFIC BLOOD RESERVOIRS:

Certain portions of the circulatory system are so extensive and/or so compliant that they are called “specific blood reservoirs.”

These include,

- The spleen, which sometimes can decrease in size sufficiently to release as much as 100 milliliters of blood into other areas of the circulation;

- The liver, the sinuses of which can release several hundred milliliters of blood into the remainder of the circulation;

- The large abdominal veins, which can contribute as much as 300 milliliters; the venous plexus beneath the skin, which also can contribute several hundred milliliters.
9. ANATOMY OF LIVER:

GROSS ANATOMY:

It is the largest mixed gland in the body performing both exocrine and endocrine functions. Situated in whole of the right hypochondrium, upper part of epigastrium, left hypochondrium. Wedge shaped reddish brown in color. Average Weight is 1.5 k.g, In Male – 1.4 to 1.8 k.g, In Female – 1.2 to 1.4 k.g, In Newborn -150 gm.

Body weight: liver ratio is,

- **In adult** - 36:1, in new born – 18:1
- **In newborn and children** - comparatively larger than adult, according to the body ratio.

*Cause:* it is due to the hemopoietic activity of liver in fetal life.

*Area occupied* – in new born children it occupies 2/5th of the total abdomen.

Characteristics:

- The liver is highly vascular organ and moves with the respiration and is soft, solid and friable to touch.
- This is essential for life. The surgical removal of two-thirds of the liver may capable of life.
- The diagnosed growth of the liver cells in cirrhosis is detrimental and produces portal hypertension.

Factors keeping the liver in position properly:

- Hepatic veins, open into the inferior venacava in the groove for IVC.
- Intra abdominal pressure which is maintained by the tone of the abdominal muscles.
- Sheaths of the blood vessels which enter and leave the liver.
- Ligaments of the liver and surrounding related structures or organs.

External Features:

It has five surfaces (1) Anterior (2) posterior (3) superior (4) inferior and (5) right.

One prominent border: Inferior border\(^6\).

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"Confirmation of Anatomical structure of Raktadhara Kala in animal model"
Blood supply of liver:

The liver receives maximum blood supply of about 1500 mL/minute. It receives blood from two sources, namely oxygenated blood from hepatic artery and nutrient rich, deoxygenated blood from hepatic portal vein. Branches of both the hepatic artery and the hepatic portal vein carry blood into liver sinusoids, which then drains into the central vein and eventually passes into a hepatic vein. Which then drain into the inferior vena cava.

Hepatic portal circulation:

- The hepatic portal circulation carries venous blood from the gastrointestinal organs and spleen to the liver.
- A vein that connects two systems of capillary bed is called as portal vein.
- The hepatic portal vein receives blood from capillaries of gastrointestinal organs and the spleen and delivers it to the sinusoids of the liver.
- The liver receives about 75% of its blood through the hepatic portal vein, with the remainder coming from the hepatic artery proper.
- After a meal, hepatic portal blood is rich in nutrients absorbed from the gastrointestinal tract. The liver stores some of them and modifies others before they pass into the general circulation.
- The superior mesenteric and splenic veins unite to form the hepatic portal vein.

Basic Histology Of The Liver \textsuperscript{68}:

- In sections through the liver, the substance of the organ appears to be made up of hexagonal areas that constitute the hepatic lobules (fig.12).
- In the transverse sections each lobule appears to be made up of cords of liver cells that are separated by sinusoids. However, the cells are really arranged in the form of plates that branch and anastomose with one another to form a network. Spaces within the network are occupied by sinusoids.
Portal canal:

- Along the periphery of each lobule there are angular intervals filled by connective tissue. These intervals are called portal canals, the canals forming a connective tissue network permeating the entire liver substance.
- Each canal contains a) a branch of the portal vein b) a branch of the hepatic artery & c) an interlobular bile duct. These three structures collectively form a portal triad. (fig.11)

Blood from the branch of the portal vein, and from the branch of the hepatic artery, enters the sinusoids at the periphery of the lobule and passes towards its centre. Here the sinusoids open into a central vein that occupies the centre of the lobule. This central vein drains into hepatic veins (which leave the liver to end in the inferior vena cava).

Fig.11. Histology of liver. a) Overview of histological components of liver.
  b) Details of histological components of liver.
Portal lobule:

- The vessels in a portal triad usually give branches to parts of three adjoining lobules.

- The area of liver tissue (comprising parts of three hepatic lobules) supplied by one branch of the portal vein is regarded by many authorities as the true functional unit of liver tissue, and is referred to as a portal lobule.

Fig.12. Scheme to show the concept of portal lobules (pink). Hepatic lobules are shaded green. Note that the portal lobule is made up of parts of three hepatic lobules.

Portal acinus

- The portal acinus is a still smaller unit, consists of the area of liver tissue supplied by one hepatic arteriole running along the line of junction of two hepatic lobules. Two central veins lie at the ends of the acinus.
Hepatocytes in the hepatic acinus are arranged in three zones around the short axis, with no sharp boundaries between them.

Cells in zone 1 are closest to the branches of the portal triad and the first to receive incoming oxygen, nutrients, and toxins from incoming blood. These cells are the first ones to take up glucose and store it as glycogen after a meal and break down glycogen to glucose during fasting. They are also the first to show morphological changes following bile duct obstruction or exposure to toxic substances. Zone 1 cells are the last ones to die if circulation is impaired and the first ones to regenerate.

Cells in zone 3 are farthest from branches of the portal triad and are the last to show the effects of bile obstruction or exposure to toxins, the first ones to show the effects of impaired circulation, and the last ones to regenerate. Zone 3 cells also are the first to show evidence of fat accumulation.

Cells in zone 2 have structural and functional characteristics intermediate between the cells in zones 1 and 3.
Glisson’s capsule:

- The liver is covered by a capsule (Glisson’s capsule) made up of connective tissue. This connective tissue extends into the liver substance through the portal canals where it surrounds the portal triads.

- The sinusoids are surrounded by reticular fibers. Connective tissue does not intervene between adjoining liver cells.

Bile canaliculi:

- Bile secreted by liver cells is poured into bile canaliculi.

- These canaliculi have no walls of their own. They are merely spaces present between plasma membranes of adjacent liver cells.

- The canaliculi form hexagonal networks around the liver cells. At the periphery of a lobule the canaliculi becomes continuous with delicate intralobular ductules, which in turn become continuous with larger interlobular ductules of portal triads. The interlobular ductules are lined by cuboidal epithelium. Some smooth muscle is present in the walls of larger ducts.

Further details of liver structure:

The liver cells are arranged in the form of anastomosing plates, one cell thick, and that the plates form a network in the spaces of which sinusoids lie. In this way each liver cell has a sinusoid on two sides. The sinusoids are lined by an endothelium in which there are numerous pores (fenestrae). A basement membrane is not seen. Interspersed amongst the endothelial cells there are hepatic macrophages (Kupffer cells). The surface of the liver cell is separated from the endothelial lining of the sinusoid by a narrow peri sinusoidal space (of Disse). Microvilli, present on the liver cells, extend into this space. As a result of these factors hepatocytes are brought into a very intimate relationship with the circulating blood. Some fat cells may also be seen in the space of Disse.

The surface of a hepatocyte can show three kinds of specialization.
A) Sinusoidal surface:

As mentioned above the cell surfaces adjoining sinusoids bears microvilli that project into the space of Disse. The cell surface here also shows many coated pits that are concerned with exocytosis. Both these features are to be associated with active transfer of materials from sinusoids to hepatocytes, and vice versa. About 70% of the surface of hepatocytes is of this type.

B) Canalicular surface:

Such areas of cell membrane bear longitudinal depressions that are opposed to similar depressions on neighbouring hepatocytes, to form the wall of a bile canaliculus. Irregular microvilli project into the canaliculus. On either side of the canaliculus, the cell membranes of adjoining cells are united by junctional complexes. About 15% of the hepatocyte surface is canalicular.

C) Intercellular surface:

These are areas of cell surface where adjacent hepatocytes are united to each other just as in typical cells. Communicating junctions allow exchanges between the cells. About 15% of the hepatocyte surface is intercellular.

![Fig.14 Three functional specialization of the cell surface of a hepatocyte.](image-url)
Liver Has High Blood Flow and Low Vascular Resistance:  

About 1050 milliliters of blood flows from the portal vein into the liver sinusoids each minute, and additional 300 milliliters flows into the sinusoids from the hepatic artery, the total averaging about 1350 ml/min. This amounts to 27% of the resting cardiac output.

Liver Functions as a Blood Reservoir:

Because the liver is an expandable organ, large quantities of blood can be stored in its blood vessels. Its normal blood volume, including both that in the hepatic veins and that in the hepatic sinuses, is about 450 milliliters, or almost 10 percent of the body's total blood volume. When high pressure in the right atrium causes backpressure in the liver, the liver expands, and 0.5 to 1 liter of extra blood is occasionally stored in the hepatic veins and sinuses. This occurs especially in cardiac failure with peripheral congestion. Thus, in effect, the liver is a large, expandable, venous organ capable of acting as a valuable blood reservoir in times of excess blood volume and capable of supplying extra blood in times of diminished blood volume.

Hemopoietic function of liver:

In the early weeks of embryonic life, primitive, nucleated red blood cells are produced in the yolk sac. During the middle trimester of gestation, the liver is the main organ for production of red blood cells but reasonable numbers are also produced in the spleen and lymph nodes. Then, during the last month or so of gestation and after birth, red blood cells are produced exclusively in the bone marrow.

Liver stores vitamin B12 necessary for erythropoiesis and iron necessary for synthesis of hemoglobin. Liver produces thrombopoietin that promotes production of thrombocytes.

Functions of liver sinusoids:

Liver endothelial cells form a continuous lining of the liver capillaries, or sinusoids, separating parenchymal cells and fat-storing cells from sinusoidal blood. Liver sinusoidal endothelial cells differ in fine structure from endothelial cells lining larger blood vessels and from other capillary endothelia in that they lack a distinct basement membrane and also contain open pores, or fenestrae, in the thin cytoplasmic projections which constitute the sinusoidal wall.
Functions:

- This distinctive morphology supports the protective role played by liver endothelium, the cells forming a general barrier against pathogenic agents and serving as a selective sieve for substances passing from the blood to parenchymal and fat-storing cells, and vice versa.

- Sinusoidal endothelial cells, furthermore, significantly participate in the metabolic and clearance functions of the liver.

- They have been shown to be involved in the endocytosis and metabolism of a wide range of macromolecules, including glycoprotein, lipoproteins, extracellular matrix components, and inert colloids, establishing endothelial cells as a vital link in the complex network of cellular interactions and cooperation in the liver.

- Fine structural studies in combination with the development of cell isolation and culture techniques from both experimental animal and human liver have greatly contributed to the elucidation of these endothelial cell functions.
7. STRUCTURE OF SPLEEN:

GROSS ANATOMY:

Definition:

Spleen is the largest ductless gland of hemolymph system acting as a filter for blood and plays an important role in the immune response of the body.

Characteristic features:

- Spleen is highly vascular, friable, and elastic organ and is purple in color.
- It is a sub diaphragmatic organ.
- Splenic parenchyma may regenerates after partial removal of it.
- Normal spleen contains approximately one – third of the total body platelets and significant number of neutrophils.
- These sequestered cells are needed in emergency condition, such as infection, inflammation, bleeding, etc.

Shape: varies from slightly curved wedge to a tetrahedron in shape.

Situation: between the fundus of stomach and diaphragm and occupies in the left hypochondrium and epigastrium.

Measurements:

Thickness -1inch, breadth – 3 inch, length – 5 inch, weight – 7 ounce, axis- left 10th rib.

Blood supply – by Spleenic artery and Spleenic vein.

74
HISTOLOGY OF SPLEEN.

CONNECTIVE TISSUE BASIS:

- The spleen is the largest lymphoid organ of the body.

- Except at the hilum, the surface of the spleen is covered by a layer of peritoneum (referred to as the serous coat). Deep to the serous layer the organ is covered by a capsule.

- Trabeculae arising from the capsule extend into the substance of the spleen. As they do so the trabeculae divide into smaller divisions that form a network. The capsule and trabeculae are made up of fibrous tissue in which elastic fibers are abundant.

- The spaces between the trabeculae are pervaded by a network of reticular fibers, embedded in an amorphous matrix.

- Fibroblasts (reticular cells) and macrophages are also present in relation to the reticulum.

- The interstices of the reticulum are pervaded by lymphocytes, blood vessels and blood cells, and by macrophages.
THE RED PULP:

- The red pulp is composed of **splenic cords** and **sinusoids**.

- The splenic cords contain a network of reticular cells supported by reticular fibers. The splenic cords contain T and B lymphocytes, macrophages, plasma cells and many blood cells (erythrocytes, platelets, and granulocytes).

- The splenic cords are separated by irregularly shaped wide sinusoids. Elongated endothelial cells line the sinusoids of the spleen with the long axes parallel to the long axes of the sinusoids. These cells are enveloped in reticular fibers set primarily in a transverse direction, much like the hoops on a barrel.

- Surrounding the sinusoid is an incomplete basal lamina. Because the spaces between the endothelial cells of splenic sinusoids are 2-3µm in diameter or smaller, only flexible cells are able to pass easily from the red pulp cords to the lumen of the sinusoids. Unfortunately, because the lumen of sinusoids in the red pulp very narrow and the splenic cords are infiltrated with red blood cells, microscopic observation of a spleen section is not always easy; observation of PALS may also be difficult.
On reaching the hilum of the spleen the splenic artery divides into about five branches that enter the organ independently. Each branch divides and subdivides as it travels through trabecular network.

Arterioles arising from this network leave the trabeculae to pass into the inter-trabecular spaces. For some distance each arteriole is surrounded by a dense sheath of lymphocytes. These lymphocytes constitute the white pulp of the spleen. The arteriole then divides into a number of straight vessels that are called penicilli. Each of the penicilli shows a localized thickening of its wall that is called an ellipsoid. The ellipsoid consists of concentric lamellae formed by aggregation of fibroblasts and macrophages. The lumen of each pennicilus is much narrowed at the ellipsoid. Distal to the ellipsoid the vessels dilates to form an ampulla the walls of which become continues with the reticular framework.
• As a result blood flows into spaces lined by reticular cells, coming into direct contact with lymphocytes here. The part of splenic tissue which is infiltrated with blood in this way is called the red pulp.

• The circulation in the red pulp of the spleen is thus an ‘open’ one in contrast to the ‘closed’ circulation in other organs. However, circulation in the white pulp, and in trabeculae, is of the normal closed type.

SINUSOIDS OF SPLEEN:

• Sinusoids in the spleen are wide vessels that drain into trabecular veins.

• Blood from the spaces of the red pulp is collected by wide sinusoids which drain into vein in the trabecular veins (largest veins inside the spleen).

• The sinusoids of the spleen are lined by a somewhat modified endothelium. The endothelial cells here are elongated and are shaped like bananas. They are referred to as stave cells.

• Endothelium lining the sinusoids mechanically filters blood cells as they enter the spleen.

• Worn-out or abnormal red cells attempting to squeeze through the narrow intercellular spaces become badly damaged, and are subsequently devoured by macrophages (are a type of WBC that engulfs and digests cellular debris, foreign substances, microbes, and cancer cells in a process called phagocytosis) in the red pulp.

• In addition to aged red blood cells, the sinusoids also filter out particles that could clutter up the bloodstream, such as nuclear remnants, platelets, or denatured hemoglobin.

• With the EM a system of ultramicroscopic fibrils is seen to be present in their cytoplasm. The fibrils may help to alter the shape of the endothelial cells thus opening or closing gaps between adjoining cells.
THE WHITE PULP:

- The white pulp is made up of lymphocytes that surround arterioles. As a result it is in the form of cord like aggregations of lymphocytes that follow the branching pattern of the arterioles. The cords appear to be circular in transverse section.
- At places the cords are thicker than elsewhere and contain lymphatic nodules similar to those seen in the lymph nodes. These nodules are called Malpighian bodies. Each nodule has a germinal centre and a surrounding cuff of densely packed lymphocytes.

SPLEEN AS A RESERVOIR FOR STORING RED BLOOD CELLS:

The spleen has two separate areas for storing blood: the venous sinuses and the pulp. The sinuses can swell the same as any other part of the venous system and store whole blood.

In the splenic pulp,

- The capillaries are so permeable that whole blood, including the red blood cells, oozes through the capillary walls into a trabecular mesh, forming the red pulp. The red cells are trapped by the trabeculae, while the plasma flows on into the venous sinuses and then into the general circulation.
- As a consequence, the red pulp of the spleen is a special reservoir that contains large quantities of concentrated red blood cells. These can then be expelled into the general circulation whenever the sympathetic nervous system becomes excited and causes the spleen and its vessels to contract.
- As much as 50 milliliters of concentrated red blood cells can be released into the circulation, raising the hematocrit 1 to 2 per cent.
- In other areas of the splenic pulp are islands of white blood cells, which collectively are called the white pulp. Here lymphoid cells are manufactured similar to those manufactured in the lymph nodes. They are part of the body’s immune system.
BLOOD-CLEANSING FUNCTION OF THE SPLEEN:

- Blood cells passing through the splenic pulp before entering the sinuses undergo thorough squeezing. Therefore, it is to be expected that fragile red blood cells would not withstand the trauma. For this reason, many of the red blood cells destroyed in the body have their final demise in the spleen.

- After the cells rupture, the released hemoglobin and the cell stroma are digested by the reticuloendothelial cells of the spleen, and the products of digestion are mainly reused by the body as nutrients, often for making new blood cells.

RETICULOENDOTHELIAL CELLS OF THE SPLEEN:

- The pulp of the spleen contains many large phagocytic reticulo endothelial cells, and the venous sinuses are lined with similar cells.

- These cells function as part of a cleansing system for the blood, acting in concert with a similar system of reticulo endothelial cells in the venous sinuses of the liver.

- When the blood is invaded by infectious agents, the reticuloendothelial cells of the spleen rapidly remove debris, bacteria, parasites, and so forth.

- Also, in many chronic infectious processes, the spleen enlarges in the same manner that lymph nodes enlarge and then performs its cleansing function even more avidly.

FORMATION OF BLOOD CELLS IN SPLEEN:

Spleen plays an important role in the hemopoeitic function in embryo. During the hepatic stage, spleen produces blood cells along with liver. In myeloid stage it produces the blood cells along with liver and bone marrow.
8. STRUCTURE OF ENDOTHELIUM:

Endothelium History:

**Wilhelm His** first introduced the term endothelium in 1865 by in an essay titled, Die Häute und Höhlen des Körpers (The Membranes and Cavities of the Body). His, a professor at the University of Basel in Basel, Switzerland, coined the term to distinguish between the cells lining the cavities of a body, especially blood vessels, and the epithelia, or layers of cells covering the outer surfaces of organs. Using microscopes, His detailed the developmental history of the membranes and cavities formed by the middle germ layer, or the mesoderm, during the early stages of development.

**Origin:** Endothelial cells and haemopoietic cells arise from hemangioblasts, blast-like bi potential cells. Precursor cells are thought to arise from the ventral floor of the dorsal aorta within the aorto – gonad - mesonephros region. Splanchnopleuric mesoderm transforms into mesenchymal cells, which differentiate into the hemangioblasts. The hemangioblasts then becomes an intermediate pre-endothelial cell, which can further differentiate into either a committed hematopoietic cell line, or an endothelial cell. Endothelial cells can also transdifferentiate into mesenchymal cells and intimal smooth muscle cells. **Structure:** The endothelium is a monolayer of flattened polygonal cells which extends continuously over the luminal surface of the entire vascular tree. Its structure varies in different regions of the vascular bed.

Endothelial cells are thin but extend over a relatively large surface area, about 4000 to 7000 square meters. In adults approximately ten trillion (1013) cells form an almost 1 kg `organ'. The endothelium is the cellular interface between the circulating blood and underlying tissue. As the medium between these two sets of tissues. Endothelial cells are generally elongated in the direction of blood flow, especially in arteries. They usually adhere firmly to each other at their edges, so that the lining of the lumen presents no discontinuity, other than in sinusoids. The thickness of endothelial cells is maximal at the level of their nucleus, where it can reach 2–3 μm, and this part of the cell often bulges slightly into the lumen. Elsewhere, the endothelial cell is thinner and laminar: in capillaries, these portions of the cell often measure as little as 0.2 μm in thickness. The shape, size, and appearance of endothelial cells, called their phenotypes, vary
depending upon which part of the body the cells are from, a property called phenotypic heterogeneity. The endothelium, its properties, and its responses to stimuli are governed largely by the local environment of the cells.

Fig. 17. Structure showing the small artery in cross section.

Fig. 18. Capillaries (A) Electron micrograph of a cross section of a small capillary. The wall is formed by a single endothelial cell surrounded by a basal lamina. (B) Scanning electron micrograph of the interior of a capillary.
1.  **GUNJA (ABRUS PRECATORIUS) DRUG REVIEW:**

1. **Vedic Period:**

   It is commonly available drug, which is extensively used in both Ayurveda and other traditional system of medicine.

   In *Agnipuran*, reference of *Gunja* is available for treating various diseases like Intestinal worms, vomiting, and fever and enhances the memory and lifespan of the man[^78].

   In Guptakala, *Vajikaranarth prayoga*. And also it is available in *Vastyayan Kamasutra*[^79].

2. **Samhita Period:**

   In *Charaka Samhita* .Sutrasthana, 24/22 explains as color of *Shuddha rakta* and *Charaka Chkitsa* 7/13 and 23 compared the *rakta gunja* to *kakanantika kusta*[^80].

   *Sushruta Samhita* mentioned it is mentioned under *Moolavisha* (su.k.2/5) and also explained in *arsha, dushyodhar, kaphaja visarpa, medoja granthi, kaphaja ghandamala, indralupta* (Su.chi.6/12, 14/8, 17/15, 18/20, 18/49, 20/25), and also in *pratisaraniya kshara*(Su.Su 11/12) And in *putan* and *andhaputan pratishedha* as a *oushad dharan* (Su.U.32/8, 34/7)^[^81].

   *Ah.chi.30/226* explains as *Shuddha arthava*. Mentioned in *shwas, arsha, udara, indralupta and galaganda*[^82].

   *Harita samhita* mentioned in *dadru, kusta, pittaja visarpa, and visha*[^83].

   *Sharanghadar Samhita* and *Yoga Ratnakar*, *gunja* was mentioned in *Maana paribhasha* for the purpose of measuring the *payyadrayas* (solid substances). One *gunja* is equal to 1 *ratti*, (125 mg)^[^84,85].
3. **Nighantu Period:**

   *Dhanwantari Nighantu*[^66]: It is mentioned in *upavisha gana*.

   *Priya Nighantu*[^67]: It is explained in *shatapushpadi varga*. *Gunja* seeds are indicated in *Vatavyadhi, Urusthambha, Vrana, Kusta*.

   *Madanapala Nighantu*[^68]: It is explained in *Abhayadi varga*.

   Here the *shodhan* process of *Gunja has been explained* by using *kanji/godugda swedana* for 3hours in *dolayantra*. Properties of *Gunja* seeds were mentioned like *keshya, balya, twachya, netrya, vrsya, kandughna, grahanashan* etc.

   *Saraswati Nighantu*[^69]: it is mentioned in *latadi varga*.

   *Raja Nighantu*[^70]: it is mentioned in *guduchyadi varga*.

   *Kaiyadeva Nighantu*[^71]:-It is explained in *aoushadhi varga*.

   Toxic symptoms like *Teevra Visha, Mada, Murcha* were mentioned. For therapeutics, it was indicated in *Indraluta, Rakshas, Graham, Kandu, Kusta, Vrana, Krimi* etc.

   *Bhavaprakasha Nighantu*[^72]:-It is mentioned in *upavisha varga*.

   The therapeutic values were explained as it is a hair tonic, antipyretic, controls dryness of mouth, vertigo, dyspnoea, thirst, stupor and indicated in eye diseases, alopecia and skin diseases etc.

   *Haritakyadi Varga*[^73]: It is explained in *guduchyadi varga*.

   *Shaligram Nighantu*[^74]: It is explained in *guduchyadi varga* and *visha varga*.

   *Rasatarangini*[^75]: It is explained under *upavisha varga, dravak gana and mitrapanchak gana*.
SYNONYMS AND THEIR MEANINGS^6:

- **Gunja** - making ratling sound when ripe.
- **Angarvalli** - looking fiery.
  - **Kaakachinchi** - looks like tamarind fruit and making ratling sound when ripe.
- **Kakananti** - making ratling sound when ripe.
- **Kakasimbi** - legumes liked by crows.
- **Krishnala** - seeds with black eye.
- **Chakrashalya** - climbing in circular way.
- **Chakrika** - seeds are in spherical in shape.
- **Durmoja** - causing loss of consciousness in high dose.
- **Bahuphala** - numerous legumes.
- **Bahuveerya** - it is potent drug.
- **Raktika, Rakta, Raktala** - seeds are red.

**Vernacular Names^7:**

- **Sanskrit** – Gunja
- **Assamese** - Latuwani
- **Bengali** - Chunhati, Gunch, Kunch
- **English** - Indian Liquorices, Jeriquity, Rosary pea,
- **Gujarati** - Chanoti, Gunja
Taxonomic Classification:\n
- **Kingdom** Plantae plants
- **Division** Magnoliophyta (Flowering plant)
- **Subdivision** Spermatophyta (Seed plant)
- **Class** Dicotyledoneae
- **Subclass** Rosidae
- **Order** Fabales
- **Family** Fabaceae (Pea family)
- **Subfamily** papilionaceae
- **Genus** Abrus
- **Species** *Abrus precatorius* Linn.
- **English Name** jequirity. Indian Liquorice root.
Morphology:

It is a woody climber; Leaves are oblong, peri-pinnate in the length of 5-7cms. Flowers are pink or whitish in color found in racemes. Each fruit pod containing 3-5 seeds which are scarlet red with a black hilum or white with black hilum or completely white. Flowering and fruiting time is autumn to winter.

Distribution and Habitat:

This plant is found all over the India, from Himalayas down to Ceylon and Siam.

Prayojya Anga: Root, Leaves and Seeds.

Rasa Panchaka:


Varieties Of Gunja:

Raja Nighantu - Shweta, Rakta and kaakaadani.
Bhavaprakasha Nighantu - Shweta and rakta.
Kaiyadeva Nighantu - Shweta and rakta.
Priya Nighantu - Shweta and rakta.
Shivadasa - Krishna and aruna.

Substitute & Adulterant: It is used as a substitute of Glyceryza glabra.
Chemical Constituents:\textsuperscript{103}:

1. **Leaves**: Contain up to 10\% glycyrrhizin, triterpene glycosides, pinitol and alkaloids such as abrine, hypaphorine, choline and precatorine, flavonoids vitexin, etc.

2. **Root**: Contains glycyrrhizin and alkaloids like abrasine and precasine.

3. **Seed**: Alkaloids are abrine, hypaphorine, choline and precatorine, abranin, pelargonidin, cyaniding, and delphinidin. Lectins. Lectins are both toxic (abrin) and nontoxic (Abrus agglutinin). Abrins are denoted by abrin a, b, c and d and consist of disulphide bond, fixed oil, steroids, flavonoids, and anthocyanins.

4. **Pericarp**: Abrine (alkaloids), abrusin, abrugenic acid, abrussic acid, etc.

**Research Profile:**

- Toxicity of *Abrus precatorius* in Nubian goats.
  
  In Abrus poisoning in appetite, bloody diarrhea, dyspnoea, dehydration, loss of condition and recumbence. The lesions were fatty change and necrosis of hepatocytes and renal convoluted tubules, pulmonary hemorrhage, edema and emphysema, and erosions of the abomasal and intestinal epithelium. The blood cell changes indicated hemo concentration\textsuperscript{104}.

- Studies on the toxicity of an aqueous extract of the leaves of *Abrus precatorius* in rats\textsuperscript{105}.
  
  The study thus showed that aqueous extract of *Abrus precatorius* is toxic and caution should be exercised in the use for medicinal purpose.

- An unusual manifestation of *Abrus precatorius* poisoning: a report of two cases\textsuperscript{106}.

- Survival after an Intentional Ingestion of Crushed *Abrus* Seeds\textsuperscript{107}.
Toxicity, distribution and elimination of the Cancerostatic lectins abrin and ricin after parenteral Injection into mice\textsuperscript{108}.

*Shodhana* (Processing) of *Gunja* (*Abrus precatorius* Linn.) Seeds with *Godugdha* (Cow’s milk); a pharmaceutical analysis in raw and *shodhita* samples indicating change in the nature of the *shodhita* drugs\textsuperscript{109}.

Purgative Activity of *Abrus Precarious* Linn. Seed Aqueous Extract in Mice\textsuperscript{110}.

This study suggests the role of seed extract of *A. precatorius* as an antifertility agent or contraceptive with a risk of DNA damage in spermatozoa and may lead to teratogenic effects\textsuperscript{111}.

Effect of *shodhan* on the toxicity of *Abrus precatorius*. the process of *shodhana* resulted in depletion of more toxic alkaloid hypaphorine and protein abrin\textsuperscript{112}.

Immunotoxins to a Human Melanoma-associated Antigen: Comparison of Gelonin with Ricin and Other A Chain Conjugates\textsuperscript{113}.

Protective Effect of *Abrus Precatorius* Seed Extract following Alcohol Induced Renal Damage\textsuperscript{114}.

A comparative antibacterial evaluation of raw and processed Gunja (*Abrus precatorius* Linn.) seeds\textsuperscript{115}.

Effect of *Abrus precatorius* L. on Experimental Tumors. The extract has a direct cytotoxic effect on the tumor cells. Vacuolation and disruption of cytoplasm accompanied by karyolysis and chromosomal abnormalities are seen in ascites tumor cells treated with the protein in vivo\textsuperscript{116}.

A Neutralizing Antibody to the A Chain of Abrin Inhibits Abrin Toxicity both In Vitro and In Vivo\textsuperscript{117}.
Acute demyelinating encephalitis due to *Abrus precatorius* poisoning-complete recovery after steroid therapy\(^{118}\).

Comparative toxicological effects of orally and intraperitoneally administered aqueous extracts of *Abrus precatorius* leaf in *Mus musculus*\(^{119}\).

Effect of *Abrus precatorius* leaves on milk induced leukocytosis and eosinophilia in the management of asthma\(^{120}\).

Hepatoprotective Activity Of *Abrus Precatorius* Linn. Against Paracetamol Induced Hepatotoxicity in Rats\(^{121}\).

Pharmacological activities of *Abrus precatorius* Linn. – A Review\(^{122}\).

*Gunja (Abrus Precatorius. Linn)* Toxicity:

**Ayurvedic perspective:**

*Gunja beeja* are highly toxic, 1 -2 seeds can produces the toxic effects. It produces *Asamashay Antra Daha* (burning sensation in stomach and intestine), *Vamana* (vomiting), *Virechana* (purgation), *Mutraghata* (retention of urine or oliguria), *Hrudayaavasad* (affects heart)\(^{123}\). In *Gunja* poisoning is *Swarasa of Tanduleeyaka (Meghanaad )* is mentioned.

**Modern perspective:**

*Abrus precatorius. Linn* Seeds are toxic, poisoning occurs due to oral ingestion of seeds or inhalation of seed powder or can be administered through injection by using Sui, which was prepared by *Abrus precatorius. Linn* seeds. Toxicity either by ingestion or inhalation or injection. It produces fatality in the dose of 90 to 120 mg\(^{124}\). Death was reported after the ingestion of one seed which was masticated well
(budavari 1989) and Abrin (Active principle) in the dose of 0.0001 mg – 0.0002 mg/kg body wt subcutaneously. The toxic effects are produced in 3-5 days\textsuperscript{125}.

Ingested seeds affect the gastrointestinal tract, the liver, spleen, kidney, and the lymphatic system. Seed extract exposure causes eye damage, conjunctivitis and blindness. By inhalation, it produces pulmonary edema etc. The poisoning symptoms are acute gastroenteritis with nausea, vomiting and diarrhea leading to dehydration, convulsions, and shock.

In the management of poisoning, Gastric emptying, inj. Anti-abrin administration and Symptomatic management has been done. Injection of 10 gm sodium carbonate and Inj.Ca. gluconate can be administered to maintain alkalinity and tremors. Hemodialysis in case of renal failure.

**Mechanism of Abrin:**

*Abrus* contains a potent toxin called abrin, it is a toxalbumin, composed of two subunits, A and B chain covalently linked through a disulfide bond. The B chain facilitates binding to cell surface receptors, allowing the entry of the A chain into cells. The A chain inactivates the 60S ribosomal subunits enzymatically to inhibit EF-1 and EF-2\textsuperscript{126}. This results in the inhibition of protein synthesis and subsequently produces cell death\textsuperscript{127}.

Abrin is a protein (toxin), because of high molecular weight (i.e., about 65 kDa) it is poorly absorbed in the digestive tract. Abrin limits the gastrointestinal absorption but can produce local GI symptoms including nausea, vomiting, and diarrhea, resulting in more serious poisonings with severe dehydration and death\textsuperscript{128}.

Inhalation of abrin is limited to the lungs with little evidence of significant systemic toxicity. The target cell for inhaled abrin is the type I pneumocyte. Abrin binds to cell surface receptors on type I pneumocytes and initiates acute alveolities and necrosis of the lower respiratory tract epithelium\textsuperscript{129}. A rapidly progressive pulmonary edema develops that produces severe hypoxia and death in exposed animals.
Based on animal studies, elimination of abrin probably occurs by the renal excretion of metabolites\textsuperscript{130}. Abrin is probably slow and limited, with the estimated half-life being about 8\textsuperscript{days}\textsuperscript{131}. Abrin is having cell killing (cytotoxic) effects on the Liver, CNS, Kidneys and Adrenal glands, typically 2-5 days after exposure. It is detectable in urine, plasma and blood.

These clinical features are dependable with abrin induced damage to vascular endothelial cells, interstitial edema, and extravasations of fluids and proteins similar to the vascular leak syndrome associated with ricin toxicity.