STANDARDIZATION OF DOSE OF ASCHOTHANA PROCEDURE

By

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Dissertation submitted to the Kerala University of Health Sciences, Thrissur

In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY (AYURVEDA)

(Ayurveda Dhanwanthari)

In

SALAKYATANTRA

Under the Guidance of

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ABSTRACT

ABSTRACT

TITLE- STANDARDIZATION OF DOSE OF ASCHOTHANA

Scholar- JESNA GOPINATH* Guide- Dr.Sreeja Sukesan MD (Ay)PhD**

Nethra roga chikitsa in Ayurveda is enriched with unique therapeutic procedures known as Kriyakalpas. Out of 7 Kriyakalpas Aschothana is the method of instilling drops of medicine in specified doses into the eyes that are kept open from a height of 2A or 3.52cm. Traditional bibliotheca regarding Aschothana reveals vast formulations of herbal combinations effective in different conditions of the eye. But modern research articles regarding eyedrops point out that the major drawback of eyedrops is the decreased bioavailability. The reason goes to the small conjunctival capacity of 30µL on comparing to the size of one drop of 0.05mL.

At the same time, classical references about doses of Aschothana are indicated as 8-10-12 bindus for Lekhana, Snehana, and Ropana types respectively. Even though Bindu and drop can not be considered as same units, the classical dose is very much high so in clinical practice maximum of 4 drops are prescribed for all kinds of Aschothana without due consideration of dosha.

Classical references especially Traditional Malayalam books used two terms known as *akshi poorana* and *akshi sechana* for Aschothana but didn't specify methodologies for these two terms. Pilot surveys showed that ancestors used so many techniques to hold the medicine in the eyes but till now in-depth study regarding this topic was not done. Hence in this study efforts have been made to standardize the dose of three kinds of Aschothana.

Methodologies – 90 volunteers are selected and grouped into healthy volunteers containing 60 people for measuring the conjunctival capacity of the eye with respect to certain influencing factors like exophthalmometric values of the eye. The second group is

subdivided into three for standardizing the doses of three types of Aschothana. Two sites were chosen- Drik Madhya and Kaneenaka sandhi as per classical references. Before doing standardization of dose, standardization of Pichu varthi using different materials and in different sizes was done. A comparison of the eyedropper bottle method with Pichu varthi is also tested. The final results were analyzed statistically analyzed in order to find the relationship between the variables.

Results and conclusion- standardization of dose of Aschothana was done as per methodology and the statistical analysis showed the role of certain factors and selection of the site of doing Aschothana are important in the determination of dose.

Key words: Kriyakalpa, Aschothana ,dose, standardization

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CONTENTS

Annexure

Acknowledgment

Abbreviations

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

INTRODUCTION

Shalakya thanthra is the branch of Ayurveda contemplating Jathrurdhva gata vikaras in detail. Among that Nethra roga chikitsa is supplemented with special therapeutic procedures known as Kriyakalpas.

The main objective of Kriyakalpa is the attainment of an effective concentration of medicament at the local site, for a specified period of time, in order to elicit a response that alleviates or eliminates the disease. There are 7 types of Kriyakalpa described in our classics along with their time of administration, the duration of the procedure, and specific formulations for each types of Kriyakalpas.

Aschothana is one of the 7 types of Kriyakalpa that can be given in the early stages of the disease for minimal vitiation of doshas. This Kriyakalpa is one of the safe and economic procedure being in use for years back. The foremost practice of Aschothana as per the classics includes the instillation of drops of medicine from 2A or 3.5cm height into the eyes that are kept open. The doses were indicated for Vata,Pitta and Kapha doshas as 10/12 and 8 bindus that are dripping from a Pichu varthi hanging from sukthi.

While comparing ocular pharmacokinetics as per modern research field, total conjunctival capacity is 30 µL and the size of one drop is .05ml. Therefore applying more quantity beyond these levels can cause decreased bio-availability of medicine. So maximum of 3 drops of medicine is prescribed for allopathic topical applications.

Even though classical compendiums have described very high doses for Aschothana, as per survey studies regarding prevalent practices of Aschothana in popular institutions in India, the actual procedure is done using maximum 3 drops only.

References regarding two terminologies only are available in the textbooks - known as *akshi poorana* and *akshi sechana* . As methodology of these two procedures are not available, a pilot survey regarding a practical experience of Aschothana among ancestors was done.

It helped to reveal high doses can be possible by methodological modifications .

But nowhere, possibility in applying classical doses and its effectiveness of Aschothana were checked. So through this study feasibility and related factors in dose determination of the three kinds of Aschothana were done.

NEED AND SCOPE OF THE STUDY

The study involves, a critical analysis of the dose of Aschothana and the role of factors influencing the dose. As per our classics, the quantity indicated for the three kinds of Aschothana is very high as the cul-de-sac of the conjunctiva cannot accommodate very large doses, and excess amounts can cause decreased bioavailability of medicine.

So the standardization of the dose of this Kriyakalpa becomes a crucial topic for discussion. An evidence-based study is necessary for each and every field of medicine, especially in Ayurvedic practice. While analyzing various researches regarding standardization of ayurvedic procedures attempts are least till now. Thus efforts has been made to standardize the dose of Aschothana through this study.

OBJECTIVES

OBJECTIVES

The research thesis entitled "Standardization of Dose of Aschothana Procedure" has been conducted with the following objectives.

1. To find the conjunctival capacity of eye
2. To standardize pichu varthi
3. To find maximum number of doses that can be accommodated in the eye for three kinds of aschothana

HYPOTHESIS

Null hypothesis

It is not possible to standardize the dose of aschothana

Alternate Hypothesis

It is possible to standardize the dose of aschothana

PLAN OF WORK

The whole work was documented as a dissertation with following headings:

1. Literary review includes

The Ocular surface- Anatomy and Physiology

Nethra Sareeram – Concepts of Nethra Sareera in Ayurveda

Detailed anatomy of ocular barriers

Ocular drug delivery

Critical analysis of Kriyakalpa with Special Emphasize on Aschothana

Exophthalmometry

Concept of Prakrithi

Chapter Eight- Standardization

2. Rationale and Relevance of the study
3. Methodology
4. Result
5. Discussion
6. Summary and Conclusion

REVIEW OF LITERATURE

Chapter One - The Ocular surface

Chapter Two – Nethra Sareeram

Chapter Three- Detailed anatomy of ocular barriers

Chapter Four – Ocular drug delivery

Chapter Five- Critical analysis of Kriyakalpa with Special Emphasize on Aschothana

Chapter Six - Exophthalmometry

Chapter Seven - Concept of Prakrithi

Chapter Eight- Standardization

REVIEW OF LITERATURE

Eye drops are the most commonly used therapeutic form among conventional methods of ocular drug delivery. Topical applications in Ayurveda are included under Kriyakalpa. Aschothana means instillation of medicated herbal eye drops from two Angula (2 inches/ 3.52 cm) height. The procedure of Aschothana was promptly used in the management of various ocular conditions with objective evidence of excellent response. Symptoms like pain, itching, foreign body sensation watering redness, and burning sensation can be eradicated by Aschothana.

Several kinds of single drugs and combinations are used in the management of discrete ocular conditions for years back. So Aschothana can be considered a common methodology for healing ailments related to the eye and it is widely practiced across India.

With an abundant resource of herbal medicine in Kerala, different formulations are available in the traditional compendiums like Sahasrayogam/Chikitsa Manjari/ Sindhu Manjari/Yogamrutham. Even though these kinds of practices were followed by rural populations for many years, the authenticity regarding its methodology and dose are still confusing.

Compared with drug delivery to other parts of the body, ocular pharmacology has met with significant challenges posed by the highly developed barriers like – the complicated anatomical structure of eyes, small absorptive surface, and transparency of the cornea, the lipophilicity of corneal epithelium, metabolism, enzymes, binding of the drug with proteins contained in tear fluid, and defense mechanisms like tear formation, blinking, and flow of the substance through the nasolacrimal duct, &low capacity of the conjunctival sac (30 µL without blinking).

The primary purpose for the development of ophthalmic therapeutics is to achieve the required drug concentration in the place of absorption and sustain it for an appropriately long time, which in turn contributes to smaller application frequency.

The market available eyedropper bottles have a capacity of 10-20 ml & the standardized size of one drop is .05ml. But the total conjunctival capacity is only 30 µL which means even a single drop of medicine cannot be accommodated on the ocular surface. Therefore, the modern ophthalmic pharmacological research field is actively focusing on new methods that can cause an increase in the bioavailability of the drug. As a part of this, various bioavailability enhancers like liposomes/ diosomes/ colloidal forms/gel forms/ dendrimers are available now.

But ayurvedic pharmacokinetics have different concepts and explanations regarding the dose and mode of action of a drug. So-many theories and logical principles are needed to explain and validate the concepts and these are entirely different from modern pharmacology.

In order to understand how Aschothana was done without causing an overflow of eyes, a pilot study was conducted in the form of a survey containing questions regarding dose, use of drugs & methods adopted to prevent overflow of the eyes. The survey helped to explore rare traditional herbal combinations as well as the policies adopted to avoid the spillage of medicines from the eyes. As these methods are not unique and are susceptible to personal variation. A detailed literary search regarding the standardized practice of Aschothana was done using online methods. But research studies regarding methodology of Aschothana are few.

One study is obtained about the prevalent practice of Aschothana among various reputed institutions in India evaluated through a survey with respect to its poorva karma, pradhana karma, and paschath karma . The study was conducted by the Department of Shalakya Tantra Of Jamnagar IPGT & RA . As per the survey, the dose of Aschothana is 1-2 drops only. The Dharana kala is said to be 5 minutes. In paschath karma mridu sweda in Kapha Vatha conditions and mallika pushpa bandhana in Pitha Raktha conditions. (1)

Major drawbacks found in the result of this study are :

- This survey didn't highlight personal variations
- The factors that can influence the holding capacity of the eye aren't addressed here.
- Calculation of Dharana Kala is not mentioned.

- Bandaging eye after Aschothana have no classical reference
- Bandaging is prohibited in pitha raktha conditions as per Susrutha Acharya

So, it is again confusing whether Aschothana is the method of holding drops in the eye till the Dharana Kala is attained or it is allowed to flow out during the time of instillation.

Therefore, validating the concepts and standardizing the procedure of Aschothana is a necessary work. To begin with detailed literature work is mandatory.

ANATOMY AND PHYSIOLOGY OF RELEVANT AREAS – MODERN ASPECTS

CHAPTER ONE - THE OCULAR SURFACE

The ocular surface encompasses a variety of structures, such as the cornea, conjunctiva, lacrimal and meibomian glands, tears, connective tissues, eyelids, eyelashes and nasolacrimal duct, all of which are connected with the trigeminal pathway and the immune system, and play a part in maintaining the homeostasis of the eye.

The ocular surface is directly exposed to the external environment, and therefore is endangered by a multitude of antigens and pathogenic microorganisms. As a mucosa, it is protected by the mucosal immune system that uses innate and adaptive effector mechanisms present in the tissue and tear film. Immune protection has two partly opposing tasks: the destruction of invading pathogens is counterbalanced by the limitation of inflammatory events that could be deleterious to the subtle structure of the eye.

The anatomical ocular surface is composed of the mucosa that lines the globe and palpebral surfaces, the corneoscleral limbus, the corneal epithelium, and the tear film. Eyelids provide mechanical protection to the ocular surface. Constant blinking of eyelids helps in renewing tear film over the surface of the cornea and mechanically remove the foreign bodies and debris from the ocular surface.(2)

EYELIDS(3)

The eyelids are important for adequate tear film distribution across the ocular surface, tear drainage, protection of ocular surfaces, and cosmesis. The eyelids also contain glands that secrete substances responsible for lubricating the ocular surface.

The eyelid skin is unique because it has no subcutaneous fat and is thus the thinnest layer of skin on the body. The skin overlying the tarsus tends to be firmly attached to the underlying tissue; whereas, the skin above the tarsal plate, in the upper lid, and below the tarsal plate, in the lower lid, overlying the orbital septum is loosely attached to underlying tissue giving rise to a potential space for fluid to collect in the setting of trauma or oedema.

Parts of the eyelid- Each eyelid is divided by a horizontal furrow (sulcus) into an orbital and tarsal part.

Position of lids -When the eye is open, the upper lid covers about one-sixth of the cornea, and the lower lid just touches the limbus.

Canthi- The two lids meet each other at medial and lateral angles (or inner and outer canthi). The lateral canthus is about 2 mm higher than medial canthus

Palpebral aperture-It is the elliptical space between the upper and the lower lid. When the eyes are open it measures about 10-11 mm vertically in the center and about 28-30 mm horizontally.

Lid margin- it is 2mm broad and divided into two parts , by the lacrimal punctum

The medial portion is called lacrimal part which is devoid of lashes or glands.

The lateral portion called the ciliary portion consists of the rounded anterior border and sharp posterior border and an inter-marginal strip.

The grey line divides the inter marginal strip into an anterior strip bearing 2-3 rows of lashes and a posterior strip on which openings of meibomian glands are arranged in a row. The splitting of the eyelids when required in operations is done at the level of grey line.

The structural framework of lid include :

1. Skin
2. Subcutaneous areolar tissue
3. Layer of striated muscle – consists of orbicularis oculi muscle with three portions orbital/preseptal/pretarsal
   Levator palpebral superioris muscle is present only in the upper eyelid.
4. Submuscular areolar tissue
5. Fibrous layer
6. Layer of non-striated muscle – the Muller's muscle
7. Conjunctiva

Glands of eyelid include- Meibomian glands ,Gland of Zeis, Glands of moll, Accessory glands of Wolfring

Blood supply

Arteries of the lids (medial and lateral palpebral) form marginal arterial arcades which lie in the submuscular plane in front of the tarsal plate, 2 mm away from the lid margin, in the upper lid and about 4 mm away in the lower lid. in the upper lid, another arcade (superior arterial arcade) is formed which lies near the upper border of the tarsal plate. Branches go forward and backward from these arches to supply various structures.

Veins.

These are arranged in two plexuses: a post-tarsal which drains into ophthalmic veins and a pretarsal opening into subcutaneous veins.

Lymphatics.

These are also arranged in two sets: the pre-tarsal and the post-tarsal. Those from lateral half of the lids drain into preauricular lymph nodes and those from the medial half of the eyelids drain into submandibular lymph nodes.

Drug permeation through the eyelid skin was much higher regardless of the drug lipophilicity. eyelid skin has a thinner stratum corneum, thereby showing lower impedance, which could be the reason for the higher drug permeation through eyelid skin.

Nerve supply

Motor nerves are facial (which supplies orbicularis muscle), oculomotor (which supplies LPS muscle) and sympathetic fibers (which supply the Muller's muscle). Sensory nerve supply is derived from branches of the trigeminal nerve such as lacrimal, supraorbital and supra trochlear nerves for upper lid; and the infraorbital nerve with infra-trochlear branch for lower lid.

CORNEA

The anterior portion of the eye is composed mainly of the cornea. It is made up of 6 layers of cells -epithelium, Bowman's membrane, stroma, Dua's layer, Descemet's membrane, and endothelium. The cornea is devoid of blood vessels and it receives nourishment and oxygen supply from aqueous and tear film.(4)

The cornea has cellular and acellular components. The cellular part is made up of epithelial cells, keratocytes, endothelial cells, Collagen and glycosaminoglycans. The layers of the cornea are:

EPITHELIUM:- consist of the non-keratinized squamous stratified layer comprising 5-6 layers of cells. Serve as an outer protective barrier, and contain flattened superficial cells,

wing cells, and a single layer of columnar basal cell separated by a 10-20nm of intercellular space. Desmosome (the tight junctions) attached cells can communicate by gap junctions through which small molecules can permeate. These desmosomes are present along the lateral wall of apical cells of the epithelium.

The superficial cells are sealed tightly by zonula occludens that prevent the permeation of low lipophilicity across the cornea. So, we can say that corneal epithelium is a barrier that prevents hydrophilic substances and macromolecules. The corneal epithelium is arranged uniformly providing a smooth regular surface and is made up of non-keratinized stratified squamous epithelium. The layers have an intracytoplasmic enzyme known as crystalline that plays an important role in maintaining the transparency of the cornea.

There is a symbiotic relationship between the corneal epithelium and the overlying endothelium of the mucin layer of the tear film. This layer is produced by goblet cells of the conjunctiva and produces hydrophilicity of tear film on each blink. The basement membrane of epithelial cells has a thickness of 40-60 nm thickness and is made up of Type 4 collagen and Laminin secreted by basal cells. The basement membrane is made up of Lamina Lucida and Lamina densa(2).

STROMA:- made up of collagen and because of its hydrophilic nature stroma offers minimal resistance to diffusion of highly hydrophilic drugs. The lamellae are arranged in layers. Each layer, lamellae are arranged parallel to each other and also to the corneal plane. The alternating layers of lamellae are at right angles to each other.

BOWMAN'S MEMBRANE:- This layer consist of an acellular mass of condensed collagen fibrils. It is about 12µm in thickness. This layer shows considerable resistance to infection and is unable to regenerate so heals by scarring.

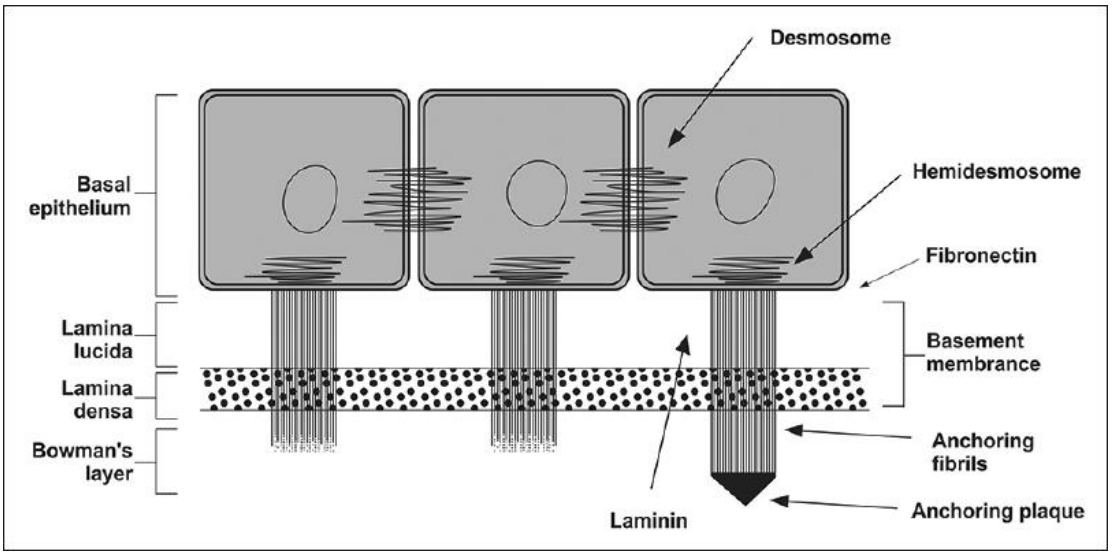
PRE-DESCEMET'S MEMBRANE:- 15µ Thick and acellular structure which is very strong and impervious to air.

DESCEMET'S MEMBRANE:- strong homogenous membrane resistant to chemical agents, trauma, and pathological processes. Descemetocele can maintain the integrity of the eyeball for a long.

ENDOTHELIUM- This layer consists of a single layer of flat polygonal epithelial cells, that appears as a mosaic pattern on slit-lamp biomicroscopy. There is a considerable degree of the functional reserve for the endothelium.

The stroma and Descemet's membrane cover the inner endothelial cells which contain macula adherens. The endothelial cells do not act as barriers due to the lack of tight junctions in between them.

Figure 4.1.1 – Barriers of cornea



APPLIED PHYSIOLOGY OF CORNEA(5)

The two primary physiological functions of the cornea are- (1) to act as a major refracting medium, (2) to protect the intraocular contents.- these functions are achieved by maintaining corneal transparency and regular replacement of tissues.

Anatomical and physiological factors play important role in maintaining corneal transparency.

Anatomical factors include- corneal epithelium and tear film, peculiar arrangement of corneal lamellae (Lattice theory of Maurice), the refractive index of corneal lamellae with variation less than 200µm, and avascularity of the cornea.

Physiological factors include- barrier function of epithelium and endothelium, the role of endothelial pumps, evaporation from corneal surface, normal IOP, Swelling pressure.

Blood supply- cornea is an avascular structure. Small loops are derived from anterior ciliary vessels invade limbal are at 1 mm

Nerve supply – long ciliary nerves which are branches of nasociliary nerves from ophthalmic division of trigeminal nerve. After going about 2 mm in cornea the nerves lose their myelin sheath and divide dichotomously and form three plexuses- stromal/ sub epithelial and epithelial

CONJUNCTIVA(6)

Conjunctiva is a translucent mucous membrane extending from lid to limbus. It lines the inner surface of eyelids and anterior surface of the sclera up to the limbus. conjunctiva help in the lubrication of eyes by generating mucus and helps with tear film adhesion. The conjunctiva consists of three parts – palpebral conjunctiva, bulbar conjunctiva, and conjunctival fornix.

The palpebral conjunctiva is further divided into the marginal, tarsal, and orbital regions. The bulbar conjunctiva is divided into scleral and limbal parts. Finally, the conjunctival fornices are divided into the superior, inferior, lateral, and medial regions. The palpebral conjunctiva lines the eyelids. The bulbar conjunctiva is found on the eyeball over the anterior sclera. Tenon's capsule binds it to the underlying sclera.

The potential space between Tenon’s capsule and the sclera is frequently used for local anaesthesia. The conjunctiva has an average thickness of 33 microns. Lastly, the conjunctival fornices form the junction between the palpebral and bulbar conjunctivas. This protective covering is loose and flexible, unlike its bulbar counterpart, allowing for movement of the globe and eyelids.

Histologically conjunctiva consists of three layers namely, epithelium, adenoid layer, and a fibrous layer.

Conjunctiva is a component of the ocular mucosal surface that provides a barrier against the external environment. The ocular mucosal surface is continuously exposed to allergens and other damaging stimuli, the specialized epithelial cells, the stratified squamous and goblet cells as well as conjunctival immune cells respond to external stimuli and protect by coordinating appropriate immune response.

CONJUNCTIVAL SAC

The conjunctiva while lining the posterior parts of the lids and anterior part of the globe forms a sac that opens at the palpebral fissure. Conjunctival sac is a narrow pocket where palpebral and bulbar conjunctiva meets in the lower eyelid, with deeper recess in the upper eyelid. It is the space between bottom of the eyelid and globe. Following topical administration the dose comes into contact with the cornea.(7)

Absorption of topically administered drug is through permeation across the cornea from pre-corneal tear film or through systemic absorption through local blood capillaries at cul-de-sac. The amount of tear fluid present in the sac is 7 microliter and the total capacity of the sac is 30 microliters. This knowledge is helpful to answer the queries regarding how many drops of eyedrops can a person put in an eye at a time.

Usually, a standard eyedropper dispenses 0.05ml per drop, so one ml contains nearly 20 drops. By calculating this way, we can easily find the fact that even one drop of eyedrop is more than enough for the eyes to hold. So it is a complete waste of eyedrop for more than one drop quantity.

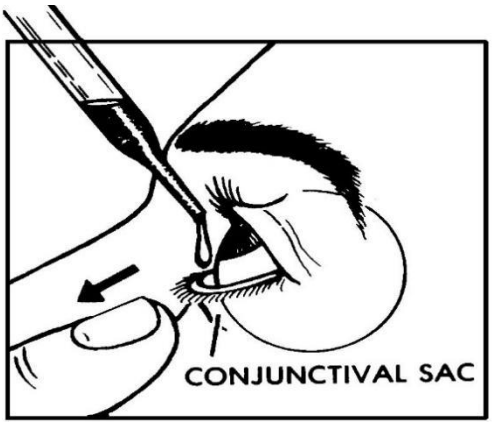


Figure 4.1.2 – conjunctival sac

Some part of topically administered drugs may absorb across the bulbar conjunctiva to the sclera and further to the uvea and posterior segment . This is an inefficient process, but may be improved by dosage forms that release drug constantly to the conjunctival surface.

The complexity of conjunctiva relies upon certain structural features present in it.(8)

1. A non-keratinized stratified squamous epithelium possessing five reported epithelial cell subtypes, including goblet cells;
2. Potential autoantigen residing basal membrane where, immune material becomes deposited in certain autoimmune diseases (e.g., mucous membrane pemphigoid) and also have a stroma mainly composed of type 4 collagen.
3. Abundant vasculature and specialized lymphoid tissue known as – Conjunctiva Associated Lymphoid Tissue (CALT)
4. Melanocyte population
5. Sensory afferent fibres derived from ophthalmic and maxillary branches of trigeminal nerve.

From a functional point of view, the conjunctiva realizes the mechanical, sensory, and immune protection of the ocular surface; the specialized secretion of fluid, electrolytes, and diverse components of the tear film. This wide range of functions makes the conjunctiva a key element in the maintenance of ocular surface homeostasis and, at the same time, quite reactive to small environmental changes and even prone to alterations

Blood supply of conjunctivae- peripheral arterial arcade/ marginal arterial arcade/ anterior ciliary arteries. Veinous supply into plexus of eyelid veins and some around cornea into the anterior ciliary veins

Lymphatics – lymphatic from lateral side drain into pre auricular lymph nodes and those from medial side drain into submandibular lymph nodes.

Nerve supply- circum -corneal zone is supplied by branches from long ciliary nerves which supply the cornea

Rest of the conjunctiva is supplied by branches from lacrimal/ infra-trochlear/ supra trochlear / supra orbital and frontal nerves.

Conjunctiva plays many roles including protection of ocular surface, production of tear film, and a conduit for drug clearance (depending on drug properties) into the systemic circulation or for drug transport to the deep tissues of the eye.

The conjunctiva, which is a moderately tight epithelium, endowed with various transport processes for the homeostasis of ions, solutes, and water in the conjunctival surface and tear film. Modulation of ion transport in the conjunctiva leads to alterations in transconjunctival fluid flow that may become useful for treatment of dry-eye state in the eye.

As a possible drug delivery route to the posterior portion of the eye, conjunctiva is an attractive route due to both larger surface area than that of cornea and expression of several key transport processes. Tear contains D-glucose and many amino acids, in addition to the usual ions in the body fluids. Several ion-coupled solute transport processes for absorption of amino acids, D-glucose, monocarboxylate, nucleosides, and dipeptides are expressed in the conjunctiva.(9)

TEAR FILM

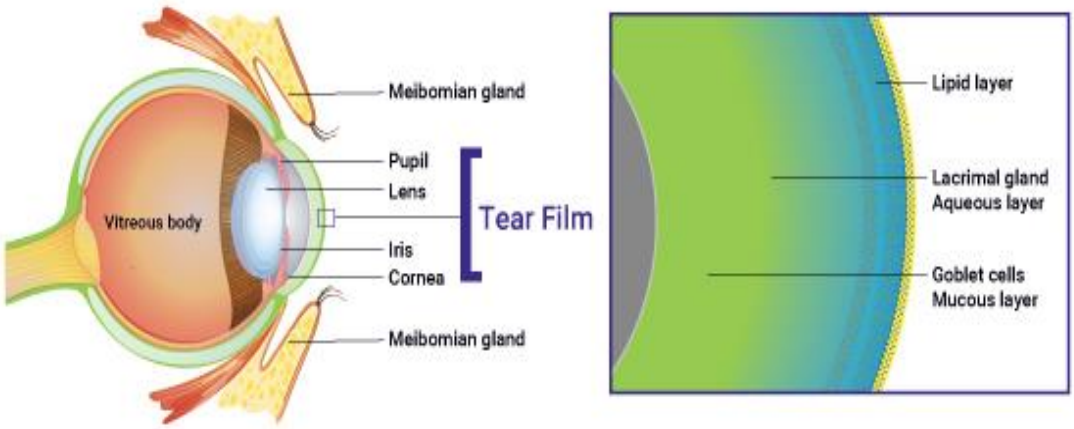
The first layer of the cornea with which light comes into contact. Tear film produces lubrication and hydration to the ocular surface. It is also a source of oxygen, immunoglobulins, lysozymes, lactoferrin, and α- and β-defensins. The tear film is composed of three layers.

The superficial oily layer is contributed by the secretions of meibomian glands. Due to its oily nature this layer floats over the top of the tear film to form a smooth refractive surface. Immediately beneath the oily layer is the aqueous layer secreted by lacrimal glands located within the conjunctival stroma. The innermost layer is the mucin layer produced primarily by the conjunctival goblet cells although the epithelial cells of the cornea and the conjunctiva also contribute.(2)

Understanding tear film dynamics is necessary for ocular topical application. Because decreased residence time at the ocular surface is the main causative factor of poor drug bioavailability. Based on anatomical and physiological aspects advancement of new techniques has been made. For example, inserts provide sustained release of drugs. Emulsions can increase drug load that may not be achievable by solution

Vehicles or ointments increase viscosity. Carriers of the drugs exist that bind to the tear film or ocular surface with greater adhesion than the drug alone.

Figure 4.1.3- Layers of tear film



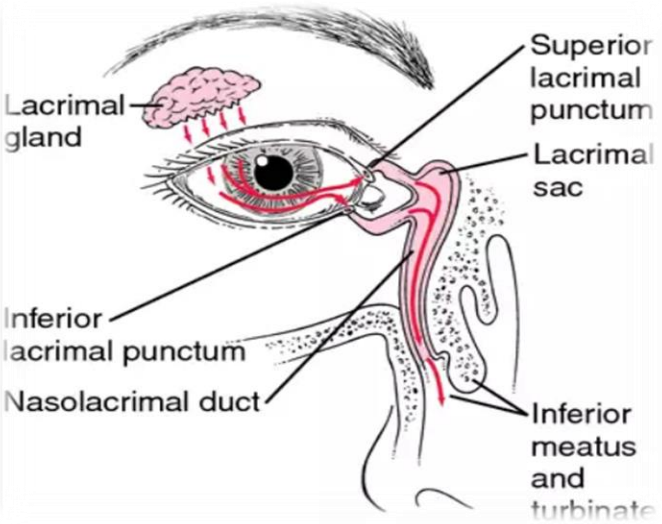
AQUEOUS HUMOUR – MAJOR PART OF BAB

Aqueous humor provides a clear colorless transparent medium between cornea and lens. The main ocular structures related to the production and dynamics of aqueous humor are the ciliary body, trabecular meshwork and uveoscleral pathway. Aqueous humor is produced at the ciliary processes and flows from posterior to anterior chamber via pupil from there it flows out through the trabecular meshwork into the schlemm's canal and subsequently into the episcleral vein via collector channels.

The blood aqueous barrier is formed by the epithelium of ciliary body and the tight capillary endothelium of iris

LACRIMAL DRAINAGE SYSTEM(10)

Figure 4.1.4 - Tear film drainage system



The lacrimal gland is an exocrine gland similar to the mammary gland and salivary gland. The gland is composed of lobules separated by loose connective tissue. Each lacrimal gland lobule consists of many acini and intralobular ducts that drain into approximately 8–12 excretory ducts or tubules. The ducts of both the orbital and palpebral lobes drain into the supero-temporal conjunctival fornix, approximately 5 mm superior the lateral tarsal border.

There are main as well as accessory lacrimal glands present. The main gland have two parts- upper orbital and lower palepabral.

Approximately 10-12 ducts pass downward from the main gland to open in the lateral part of superior fornix. One or ,two ducts also open in the lateral part of inferior fornix.

Glands of Krause and Wolfring are the accessory lacrimal gland

The arterial blood supply to the lacrimal gland comes from the lacrimal branch of the ophthalmic artery, a branch of the infraorbital artery, and occasionally from a branch of the recurrent meningeal artery. The lacrimal artery passes through the gland to feed the upper and lower eyelids. The lacrimal vein follows the course of the artery and drains into the superior ophthalmic vein.

Sensory supply from trigeminal, sympathetic from carotid plexus and the secretomotor is derived from pons via greater petrosal/ zygomatic and lacrimal nerve.

The next part in the drainage of lacrimal fluid is the Lacrimal puncta which is a small rounded opening one at upper and other at lower lids. superior and inferior canaliculi join the puncta to the lacrimal sac. Each canaliculus has two parts: vertical (1-2 mm) and horizontal (6- 8 mm) which lie at right angle to each other. The two canaliculi may open separately or may join to form common canaliculus which opens immediately into the outer wall of lacrimal sac. A fold of mucosa at this point forms the valve of Rosenmuller which prevents reflux of tears.

Next structure is Lacrimal Sac which is located in the lacrimal fossa in the anterior part of medial orbital wall. When distended, lacrimal sac is about 12-15 mm in length and 5-6 mm in breadth with a volume of about 2 cc.

Naso lacrimal duct (NLD) arises from neck of lacrimal sac to inferior meatus of the nose. It is 15- 18 mm long and lies in a bony canal formed by maxilla and the inferior turbinate. The valve of Hasner, which is present at the lower end of the duct and prevents reflux from the nose.

CONTRIBUTIONS OF LACRIMAL GLAND TO OCULAR SURFACE HEALTH(11)

Mainly tear film is the principle protecting factor of ocular surface from invading pathogens. IgA secreting plasma cells are located within the lacrimal gland itself. They help in proliferation and multiplication of helper T cells for immune related changes. Lacrimal gland also secretes antifungal and bacterial agents like lysozyme, peroxidase, tear-specific pre-albumin, psoriasin, and lactoferrin into the tear film. These substances greatly reduce susceptibility of the ocular surface due to cytotoxicity to invading pathogens.

The second major contribution of the lacrimal gland is in the aqueous produced by acinar cells that add significant volume to the tear film. The fluid is transported from the

interstitial space into the lumen of the gland by way of osmosis and released onto the ocular surface.

The lacrimal gland is also responsible for producing several other proteins and products necessary in growth and maintenance of host tissue found in the tear film. Several of these proteins are growth factors. They include epidermal, fibroblast, hepatocyte, keratinocyte, and transforming growth factor-β. Retinol, a vitamin A derivative, is also secreted by the lacrimal gland. Retinol is required in maintenance of goblet cells within the conjunctiva and controls corneal epithelial desquamation, keratinization, and metaplasia.

LACRIMAL FLUID BARRIER(12)

After instillation, the flow of lacrimal fluid removes instilled compounds from the surface of the eye. The lacrimal drainage system passes liquid from the eye to the nose. Liquid enters the puncta, two drainage points located on the posterior of the eyelid margin, one on the upper and one on the lower lid. These pass the liquid to the canaliculi, tubes that eventually fuse before meeting the lacrimal sac. The lacrimal sac can store some fluid and connects to the nasolacrimal duct which allows fluid to exit the nose by way of the inferior turbinate. Even though the lacrimal turnover rate is only about 1 µL/min the excess volume of the instilled fluid is flown to the nasolacrimal duct rapidly in a couple of minutes.

Another source of non-productive drug removal is its systemic absorption instead of ocular absorption. Systemic absorption may take place either directly from the conjunctival sac via local blood capillaries or after the solution flow to the nasal cavity. Drug absorption into the systemic circulation decreases the drug concentration in lacrimal fluid extensively. Therefore, constant drug release from solid delivery system to the tear fluid may lead only to ocular bioavailability of about 10%, since most of the drug is cleared by the local systemic absorption anyway.

Corneal epithelium limit absorption of drug from lacrimal fluid. The epithelial cells which migrate from limbal area to cornea form tight junctions and limit paracellular transport of drug. So lipophilic drugs have at least an order of magnitude of higher permeability in the cornea than the hydrophilic drugs. In general, the conjunctiva is more leaky epithelium than the cornea and its surface area is also nearly 20 times greater than that of the cornea.

Drug absorption across the bulbar conjunctiva has gained increasing attention recently, since conjunctiva is also fairly permeable to the hydrophilic and large molecules. Therefore, it may serve as a route of absorption for larger bio-organic compounds such as proteins and peptides. Clinically used drugs are generally small and fairly lipophilic. Thus, the corneal route is currently dominating.(12)

CHAPTER TWO – NETHRA SAREERAM

Nethra is most important among the five sense organs in the human body. Acharya Charaka had described the importance of eye very clearly. (13)

Nethra- uthpathi

Acarya Caraka – Nethra is developed during third month of life.(14)

Videha – Eyes are the first organ to develop in humans(15)

Acarya Susrutha – Eyes as well as all the other sense organs are formed in subtle form at foetal life itself.

Synonyms of Nethra include- nayanam/ lochanam/ chakshu/ Drishti/ akshi(16)

AKSHI- Source of reaching or seeing. As+kshi means which grasps objects.

CHAKSHU- responsible for sight.

DRISHTI- source or tool with which one sees the world.

LOCHANA- according to Amarakosa this has the capacity to see.

NETHRA- which takes or drives one toward knowledge.

Acharya Susruta has described gross ocular anatomy in first chapter of uttara-tantra in relation to their shape, size of various anatomical components. Sushruta has explained seventy-six different kind of eye diseases and their treatment in uttara tantra of Sushruta Samhita in 2nd AD.(17)

Situation - Shira (head) is chief among all organs. It is the region of the body where vital centres and all senses (indriya) of a living-being are located. Acharyas have considered it is the principal organ among all organs and organelles.

Shape - the shape and dimension of Nayana Budbudam (eye ball) as Suvrittam and Gostanakaram. Suvrittam means spherical from all sides. Gostanakaram means shaped like that teat of the cow (oval shape).

Measurements - - Acharya Sushruta has given the term Nayana budbuda for eye ball. Sushruta has explained the dimension of eyeball in terms of angula and one angula is equivalent to the central part of the patient's own thumb. Two angula is the antero-posterior diameter of the eyeball. Vertical and horizontal diameter is two and half angula(18)

In modern perspective, dimension of an adult eyeball is as follows anteroposterior diameter 24mm, horizontal diameter 23.5mm, vertical diameter 23mm, circumference 75mm, volume 6.5ml and weight 7gm(19)

Table 4.2.1 -PANCHABHOUTHIKATHVA OF OCULAR SURFACE(20)

PARTS OF NETHRA	MAHABHOOTHA	PART OF THE EYE
Krishna	Vata	Cornea
Sita	Jala	Sclera and Conjunctiva
Asru Marga	Akasa	Lacrimal Passage

Table 4.2.2 -MANDALA related to ocular surface(21)

Pakshma	Eye lashes and lid margin
Vartma	Eye lids
Sukla	Sclera
Krishna	Cornea

SANDHI related to ocular surface(22)

Junction between patalas are called as sandhi. They are 6 in number. The topical application are done along these sandhis.

Table 4.2.3 – SANDHI RELATED TO OCULAR SURFACE

Pakshma vatma sandhi	Lid margin
Vatma sukla sandhi	Fornices
Sukla krishna sandhi	Limbus
Krishna Drishti sandhi	Pupillary margin
Kaneenaka sandhi	Medial canthus
Apanga sandhi	Lateral canthus

While critically analyzing Netra Sharira deals with three major portions of eye-Mandala, Sandhi and Patala. Mandalas are 5 in number. Ocular surface is related to pakshma, vartma , sukla and krishna mandala.

Pakshma mandala is the first and outermost mandala of the eye formed by the pakshma or eyelashes. Pakshmani means chakshua achadana romani. (23)Pakshma are situated in lid margins called pakshmashaya or pakshma sadana. Pakshma is a form of kesa and can be considered as an upa-dhathu of majja.

The Upper and Lower eyelids together form a circular structure in front of the eyeball is called as vartma mandala. The eyelids are mobile tissues curtains placed in front of the eyeballs. Vartma mandala is made up of eyelids and is known as AKSHI KOSA indicating its protective function. The two eyelids meet at two points known as kaneenaka and apanga- the inner and outer canthus respectively.(16) The movement of eyelid known as nimesha and unmesha are controlled by Nimeshana unmeeshini sira controlled by vyana vayu (24).

Sukla mandala it is the part of sclera covered by conjunctiva. This mandala is present exactly inside of the vartam mandala and beyond the krishna mandala. The shukla mandala appears white in color. The shukla mandala can be allied with the scleral part of the external fibrous coat of the eyeball. Sukla mandala forms sandhi with neighbouring mandalas as

follows : peripherally it is related to vatma, medially with kaneenaka and laterally with apanga.

Krishna mandala is cornea which is transparent but appears to be black due to the underlying iris.

While looking through sandhi, these are the junctional areas between mandala.

Pakshma vartma sandhi can be considered as lid margin. The place where Anjana Kriyakalpa is applied.

Vatma sukla sandhi is fornix of conjunctiva. Mucin secretory glands like goblet cells, crypts of Henle, glands of manz, secrete mucus which is important for wetting the cornea and conjunctiva.

Conjunctiva represent the first barrier to posterior segment drug targeting so once bulbar conjunctiva is crossed the drug can diffuse through sclera into uvea and RPE to reach neural retina and vitreous humor. Additionally, it is important to underline that blood and lymphatic vessels, present in the conjunctival tissue,are responsible for unavoidable systemic absorption.(25)

Krishna sukla sandhi is limbal area. The inner and outer canthi – kaneenaka and apanga are also related to topical drug pharmacokinetics.

PATALAS – layers of eye ball (25)

Acharya sushruta has described the patala are most important structure of netra sharir. It can be appeared like as a layer of the eyeball or film or coating over the eyes. The two patala are present in the eyelids and the other four Patala in the internal eye ball. Out of them the first Patala (outermost) subsists in the tejas and jala, second Patala in the mansa (muscle), third Patala in the meda (fat), forth Patala in the asthi. Their thickness of entire patala is equal to one-fifth of pupil. The pathogenesis of Drishtigata roga, has delineate in terms of involvement of successive patala. The prognosis of the disease also depends upon the involvement of respective patala.

CONTENTS OF ORBIT- akshi bandhana

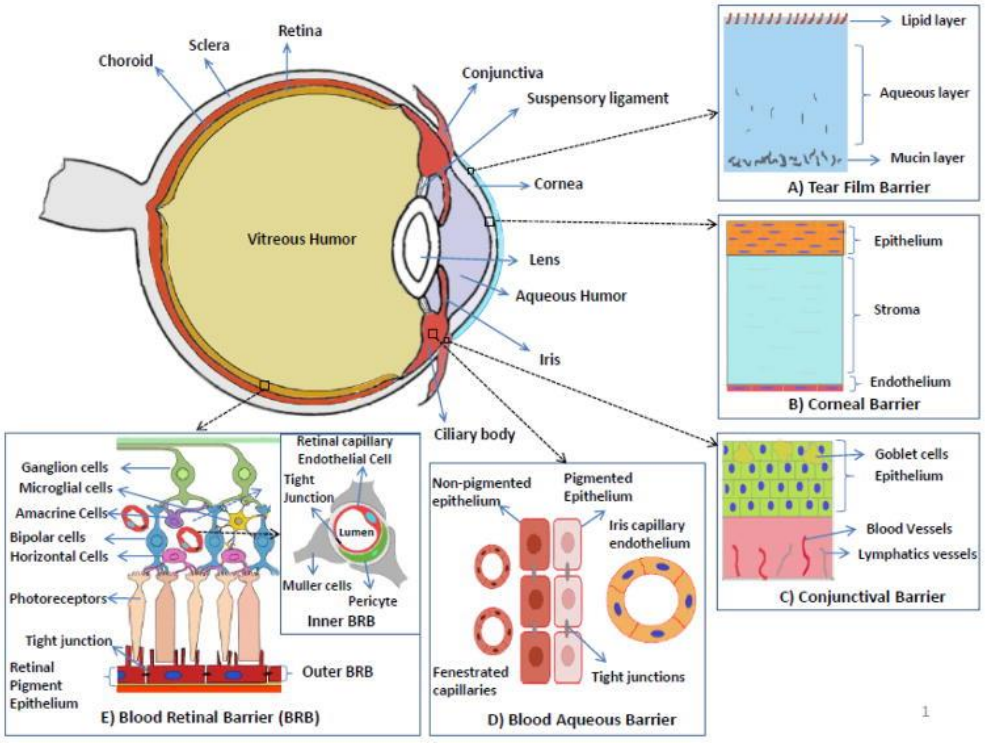
The both eyeballs are held in position by the inherent properties of the sira (veins, arteries and nerves), kandara (tendons and ligaments), meda (orbital fat), Kalakaasthi (fascia that is attached to the bony cavity) and Sleshma bandana (especially the eye ball is supported by the orbital fat) kapha as well as by the lining mucous membrane along with its vessels next to the cartilage. The vessels, ligaments, bones and joints if the living beings have strength because they are covered by the muscles

According to Sasilekha commentary of Acharya Indu, the first patala consists of sira guna, the qualities of teja and jala are also seen here. The second Patala has kandara guna which is derivative of mamsa dhatu. The third Patala has meda guna; exact visual perception takes place in this patala as dristi is seated in medas, kalakasthi remains outside meda

CHAPTER THREE – DETAILED ANATOMY OF OCULAR BARRIERS

Barriers in ocular pharmacology include anatomical, physiological and blood ocular barriers.

Figure 4.3.1 – different types of ocular barriers



Anatomical barriers

Every topical application is administered via corneal or non corneal routes.

While considering cornea as already mentioned in chapter one, composed of 6 layers. Of these epithelium of cornea act as the principal barrier. Especially to hydrophilic substances transport through intercellular spaces. Epithelial layer consists of tight junctions of corneal epithelium known as zonula occludens. The stratified squamous epithelium of cornea consists of 6 layers. A basal layer of columnar cells, two-three layers of wing shaped cells, one or two layers of squamous cells. Superficial layer contain tight junctions which act as barriers to paracellular drug absorption via tight anastomotic strands. There are four types of barriers- ZO-1,ZO-2, cingulin,and occluden. Among this occluden is the most important

one. The permeability levels of intracellular and extracelluar calcium levels influence permeability of molecules. The pores of corneal epithelium are negatively charged and so positively charged molecules are permeated fastly(26).

On the other hand stroma of cornea composed of multiple layers of cells , hexagonally arranged collagen fibers containing aqueous pores allow hydrophilic substances easily to pass through it, but significantly limit the entry of lipophilic drugs.

The remaining layers are leaky enough and don't have much role in permeability.

So in order to have a minimum bioavailability the drug should have right balance between lipophilicity and hydrophilicity.

Non corneal route mainly consist of conjunctiva and sclera. Conjunctiva is more permeable to hydrophilic substances than cornea due to much lower expression of tight junction proteins relative to corneal epithelium. The conjunctival epithelium is a tight barrier against passive entrance of substances but has also transport- and secretory functions. Ocular surface is in direct contact with external environment , and conjunctival epithelium act as a tight barrier to seal the ocular surface to prevent uncontrolled entry of any foreign bodies.

Apart from sealing function, conjunctiva also have transport and secretory function. Transport of IgA- the main protein of tear film , produced by the lamina propria and are transported through epithelium. The aquaporin channels and ion pumps of the epithelium contribute the transport of water.

The secretion of lubricant materials like lubricin and mucin that reduces the friction of ocular surface also occurs within the conjunctival epithelium.

Non corneal route have significant role in transportation of large molecules such as peptides & Proteins.

Physiological barriers

include

1. Reflex blinking
2. Tear turn over
3. Naso lacrimal drainage
4. Efflux pumps

Tear film is the primary level of defense mechanism in eye. Bioavailability of drugs further depended upon solution drainage, tear dilution, tear turn over, and increased lacrimation.(26)

REFLEX BLINKING

Reflex blinking while application of medicine into the eye significantly reduce the overall amount of medicine available for therapeutic action. An average volume of 39µL amount of eyedrop is transmitted into the eyes by using dropper bottle method. However eye can hold a volume of 30µL of volume so obviously rest of the amount get drained by nasolacrimal drainage or reflex blinking (5-7blinks/min). This can cause decreased availability of overall drug for metabolism (26)

TEAR TURN OVER

It is the phenomenon that cause great impediment to topical drug bioavailability. On application of eyedrops, cul-de-sac volume increases that leads to reflex blinking and increased tear secretion, resulting in rapid loss of medicine from precorneal area. The process continues until cul-de-sac volume returns to normal range(7-9µL).(26)

NASO LACRIMAL DRAINAGE

The naso lacrimal drainage system consist of puncta, canaliculi, lacrimal sac, and nasolacrimal duct. Histologically, the walls of the lacrimal sac and the nasolacrimal duct are vascularized, and hence are potential sites for systemic drug absorption. After topical

application, the drug remain contact with the ocular tissues for 1-2 minutes due to constant secretion of lacrimal fluid. Approximately half of the drug flows into the upper canaliculus and the rest into the lower canaliculus of the lacrimal sac. The flow further opens into the nasolacrimal duct, and, from there, drains into the nose Largely instilled volume easily get absorbed into nose via nasolacrimal drug and small dose get eliminated via nasolacrimal duct very easily. The lacrimal fluid is isotonic aqueous solution containing a mixture of proteins such as proteins and lipids. The drugs administered need to be isotonic and non-irritating to prevent significant precorneal loss.(26)

EFFLUX PUMPS

These pumps are located at apical or basolateral membrane, depending upon localization they either enhance or restrict drug absorption. Mainly two efflux pumps are responsible for drug resistance. (a) p- glycoprotein (b) multidrug resistant protein (MRP) (26)

P glycoprotein confers to resistance to accumulation of drug in multidrug resistant cells. P-gp is shown to present on the ocular conjunctival epithelial cells, ciliary non-pigmented epithelium, human cornea, iris and ciliary muscles and retinal capillary endothelial cells. MRP is detected at human corneal epithelium at the level of mRNA . This pump act as a transporter of glutathione, cysteinyl leukotrienes, glucuronides, sulfate conjugates and bile salts(26).

Blood-ocular barriers

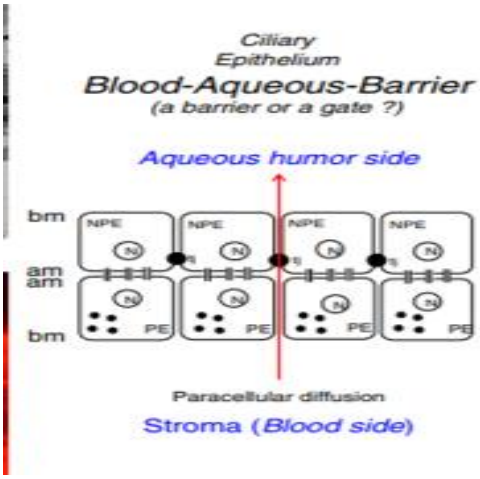
Blood aqueous barrier (BAB) and blood retinal barrier (BRB) like any other protective mechanism in our body, contain immune privileged sites that give protection from entry of foreign substances. These ocular barriers are formed by tight junctions between specific epithelial cells and vascular endothelial cells. The uveal tract plays key role in maintaining the blood-ocular barriers. Diseases involving destruction of uvea leads to exudation of excess amount of proteins or cells into aqueous humor, vitreous, or subretinal space.

Blood aqueous barrier and blood retinal barrier have distinct tissue localization, immunologic properties and physiological functions.

Blood aqueous barrier is established by the tight junction complex of proteins and adapters between non pigmented epithelial layer of ciliary epithelium, tight junctions between vascular endothelial cells in ciliary processes, in the iris vasculature, inner cells of endothelium of schlemm's canal. BAB is not a completely skewed barrier but rather it serve as a selective barrier in cell trafficking. The main patrolling of BAB is by leukocytes. The regulatory mechanisms of epithelial and endothelial cells of BAB block cytotoxic T-lymphocytes, natural killer cell functions, and promote immune deviation.

Tight junctions include adherens junctions (cadherin-catenin and nectin-afadin complexes) and gap junctions (i;e connexins). These junctional complexes respond rapidly to pharmacologic agents and physiological changes.

Figure 4.3.2 – Blood aqueous barrier



The blood retinal barrier (BRB) is established as two sections in the posterior segment of eye. Outer BRB formed by tight junctions between RPE and fenestrated choriocapillaris. The inner BRB is formed by tight junctions between non fenestrated capillary endothelia covered by astrocytes, and muller cells.

Many factors are responsible for poor drug bioavailability in topical applications

Pre-corneal fluid drainage - it is one of the major reason of low ocular drug absorption. After instillation major portion of the drug get drained into naso lacrimal duct. Several factors are known to cause this drainage

Instilled volume- higher the volume greater is the rate of drainage from the conjunctival sac.

Physiologic pH - of tear fluid is 7.4 , acidic or alkaline pH can cause excessive tear production and secretion

Tonicity of the drug- the drug can alter the normal physiological process so ophthalmic preparations should be isotonic with tear. The increased tonicity of topical application get diluted by tears. Sometimes tears can dilute the tonicity by osmosis

Viscosity of the used liquid- increasing the viscosity of the instilled dose can increase the residence time in conjunctival sac.

After administration the drug pass through cornea, then transferred into the anterior chamber. Then it get moved into the aqueous flow and by diffusion into the blood stream via anterior uvea.

Permeation of drug across the cornea happen via two pathways transcellular pathways for lipophilic drugs and paracellular pathway for hydrophilic molecules.

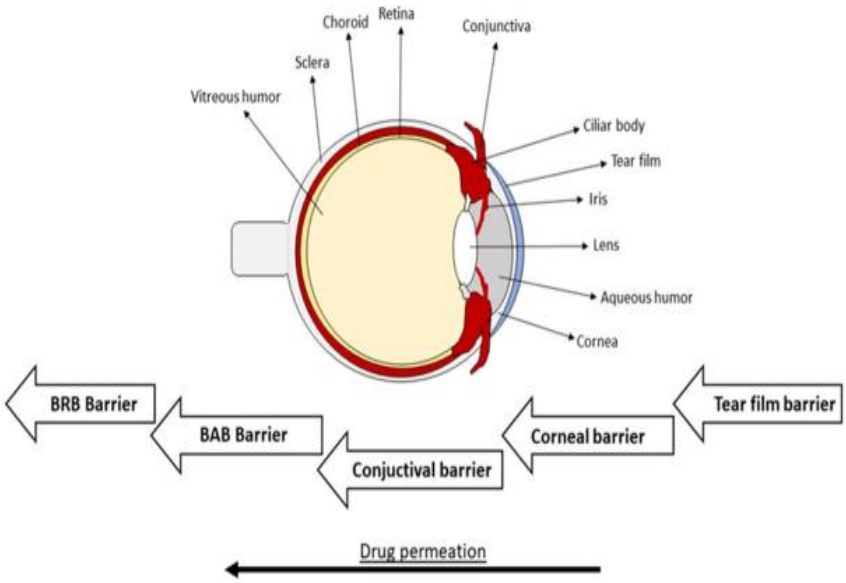
As per modern researches regarding the size of eye drop and size of cul-de-sac of conjunctiva the maximum size of the conjunctival cul de sac and tear may go upto 30µL and that size is not able to hold the 40-70µL sized average topical preparation. Considering the major drawback of anterior segment drug delivery system- lack of bioavailability, modern researches are directed at novel systems of drug delivery that help in sustained release of drug into the eyes. For achieving that drug molecules should be capable to circumvent the protective physiological barriers without causing damage to the ocular tissue.(26)

Administration of drug using a dropper bottle is somewhat challenging to old patients due to the lack of physical acuity and inability to aim adequately. The adherence to antiglaucoma therapy using eye drops deteriorates with age. Nanocarriers, such as liposomes, micelles, microemulsions, biodegradable nanoparticles, nanosponges, punctal plugs, and dendrimers hydrogels have been investigated as carriers for antiglaucoma drugs for their ability to deliver drugs in a sustained manner.

CHAPTER FOUR

OCULAR DRUG DELIVERY

Figure 4.4.1 - ocular drug delivery



Drug delivery to the eye is supposed to be one of the challenging tasks to pharmaceutical scientists. The unique anatomy and physiology render it a highly protected organ and the protective mechanisms prevent an easy entry of drug into the target site of action. Generally, we can classify ocular drug delivery into anterior and posterior segments. Drug delivery into anterior segment typically involves solutions, suspensions, and ointments which composed of 90% of marketed ophthalmic solutions however topical applications have poor ocular bioavailability due to various precorneal, static, and dynamic ocular barriers.

In addition to that size of the drop, physicochemical properties of the vehicle used, concentration of the preparation are the main factors that can affect the action of topical preparations. Lipophilic drugs are absorbed through cornea whereas lipophilic and hydrophilic drugs are able to penetrate via conjunctiva and sclera. Drug delivery to posterior segment is still a challenging task to pharmaceutical research field.

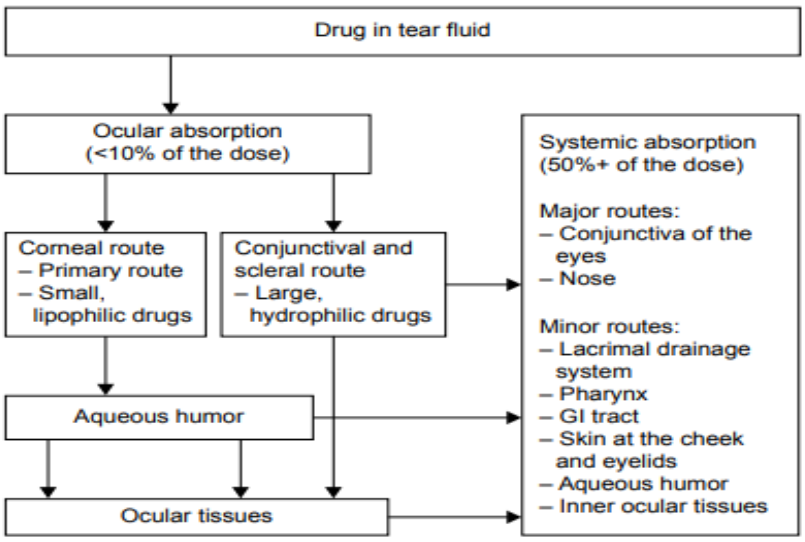
Figure 4.4.2-different drug absorption and their elimination routes are as follows :

Absorption area	Drug
Cornea	Lipophilic drugs
Conjunctiva, sclera	Lipophilic and hydrophilic drugs
From the blood via the blood–ocular barrier	Lipophilic drugs
From the blood via the blood–retinal barrier	Lipophilic drugs
With lacrimal fluid via the trabecular meshwork and Schlemm's canal	Hydrophilic and lipophilic drugs
With lacrimal fluid via venous blood flow to the front uveal tract	Lipophilic drugs
Out of the vitreous humor via the blood–retinal barrier (back route)	Lipophilic drugs
Out of the vitreous humor via the anterior chamber of the eye (front route)	Hydrophilic and lipophilic drugs

Due to ease in administration, low cost and patient compliance topical applications are more useful now. Amongst the various topical forms, eyedrops are supposed to be the most -safe, immediately active, and non-invasive method. ocular drops are supposed to provide medicine into anterior segment. But most of them do not offering adequate bioavailability to the target site due to wash off drugs from eye by various mechanisms like nasolacrimal drainage, tear dilution, tear turnover, tissue integrity of cornea and patient related factors

like positioning while applying the medicine. Among this tear turn over contribute majority to the poor bioavailability of ocular drops. Normal healthy eyes have a tear volume of nearly 7-9 microliter and turn-over rate 0.5-2.2microliter per minute. The average volume of major formulations measures around 56 micro liter and the excess amount drains via naso-lacrimal duct into systemic circulation. Conjunctival circulation also offers barrier function to the eyedrops absorption. (26)

Figure 4.4.3 -The possible absorption pathways of topical applications can be summarized as :



Due to these reasons frequent dosing is required to ensure desired therapeutic effect which may cause discomfort and inconvenience to the patient. In case of chronic posterior segment pathologies oral alone or in combination with topical forms produce desired effect. But large doses can cause systemic side effects.

Still, ocular topical application remains one of the important ways of anterior segment approach. It is simply because of the ease of administration, comparatively low cost and patient compliance.

PRE- MEASURES TO IMPROVE BIOAVAILABILITY OF EYE DROPS

Two major routes of absorption have been proposed for drugs instilled via topical methods. They are corneal route and non-corneal routes. Corneal route is via cornea-aqueous humour and intraocular tissues. Non corneal route is by conjunctiva-sclera- choroid/retinal pigment epithelium. The preferred mode of absorption depends upon the physicochemical properties of the permeant.

A. The driving force for passive diffusion of drug across cornea depends on the concentration of drug available in the precorneal area. However, for efficient ocular drug delivery with eye drops, high corneal permeation with longer drug cornea contact time is required.

B. To improve drug contact time, permeation and ocular bioavailability different additives may be used along with topical applications like- viscosity enhancers, permeation enhancers, and cyclodextrins.

C. Pre-corneal residence time and bioavailability are added by the use of viscosity enhancers such as hydroxy methyl cellulose, hydroxy ethyl cellulose, sodium carboxy methyl cellulose, , hydroxypropyl methyl cellulose and polyalcohol.

D.Corneal integrity can be modified by the use of permeation enhancers. Chelating agents, bile salts, preservatives and surface active agents are some of the permeation enhancers.

E.Addition of permeability enhancers ocular bioavailability but some of them found to be locally toxic to the tissues. So modified methods are being used now after several research methods. Polycarbophil-cysteine is an example which is used as an excipient that did not damage the corneal tissue integrity and suggested that it could be safe for ocular formulations.(27)

LIMITATIONS OF ORAL MEDICINE

Oral administration is not advisable and may be highly beneficial only if the drug possess high oral bioavailability. In addition, molecules in systemic circulation should be able to

cross BAB & BRB blood aqueous barrier and blood retinal barrier respectively after oral administration. Blood aqueous barrier is present in the anterior segment and consists of two distinct cell layers- the endothelium of iris/ ciliary blood vessels and non-pigmented ciliary epithelium. Both layers prevent drug entry into intraocular tissues including aqueous humor, due to the presence of tight junctions.

By summarizing the pharmacokinetics of ocular topical applications are supposed to be occur in the following ways.

- Trans-corneal permeation from the lacrimal fluid into the anterior chamber.
- Non-corneal drug permeation across the conjunctiva and sclera into the anterior uvea.
- Drug distribution from the blood stream via blood-aqueous barrier into the anterior chamber.
- Elimination of drug from the anterior chamber by the aqueous humor turn-over to the trabecular meshwork and sclemm's canal.
- Drug elimination from the aqueous humor into the systemic circulation across the blood-aqueous barrier.
- Drug distribution from the blood into the posterior eye across the blood-retina barrier.

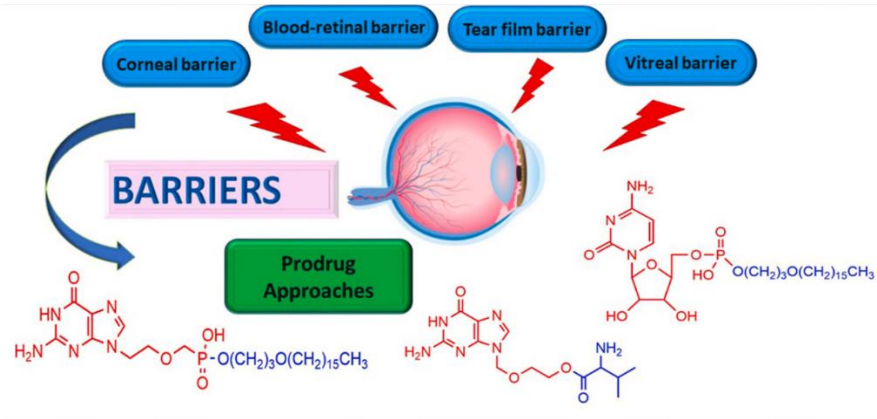
PRODRUG STRATEGIES FOR INCREASING OCULAR DRUG ABSORPTION

Ocular pharmacokinetics is a highly research oriented area to develop strategies that circumvent the associated barriers in ocular drug delivery and thereby to achieve better clinical output. The viable strategies to enhance bioavailability of ocular therapeutics include- formulating the drugs as solutions, suspensions, gels by physical methods or by using chemical methods like development of prodrugs.

Prodrugs are enzymatically or chemically transformed in vivo derivatives of bio-diversible main drugs itself. On transformation they have the capability to derive the parent molecule. Prodrugs can increase physiochemical, biochemical and pharmacokinetic properties of ophthalmic drugs. Studies have shown that these prodrugs can chemically and

metabolically increase the drug shelf life, solubility and stability. Thus, can provide desired therapeutic effect in target tissues without much side effects.

Figure 4.4.4 – barriers in ocular drug delivery and prodrug approach



Designing of prodrugs which accomplishes most of the criterias of an ideal drug is a challenging task

The important considerations while designing a prodrug include :

- The pro drugs must be safe and non toxic
- Pro drug must possess sufficient shelf life and stability in final formulation
- Majority of ocular applications are in the form of aqueous solutions so water solubility of a prodrug is important especially the parent drug is lipophilic and possess low water solubility.
- The lipophilic property of prodrug should be minimum in order to accomplish higher diffusion across lipophilic ocular barriers.
- The ability of prodrug to evade the biopharmaceutical and physicochemical properties (of the parent drug) should be high or satisfactory enough

The common functional groups that have been used in prodrug design include- carboxylic, hydroxyl, amine, and carbonyl groups. Modification of these functional groups which includes esters , carbamates , phosphates and oximes.

ESTER PRODRUGS

The most common eyedrops formulated with prodrugs belongs to esters derived from COOH or OH functional groups. Usually these COOH / OH functional groups exist in ionized form under normal physiological conditions that doesn't allow the passage through a membrane containing lipids. But proper esterification of active molecules with other pro drugs can generate ester derivatives that have adequate level of lipophilicity and hydrophilicity. With the help of esterases present in the eyes the ester derivatives of the drug can be converted into active drug. Ester prodrugs can enhance corneal penetration and improved therapeutic index.

CARBAMATE PRODRUGS

Carbamate prodrugs can be prepared from amine carboxyl functional groups. But they are very rarely used in ophthalmic preparations. Because these prodrugs have little stability they have limited use only.

OXIME PRODRUGS

These are derivatives of ketone. The long standing IOP lowering effect as well as high therapeutic index make oxime prodrugs more efficient.

LIPID PRODRUGS

Lipid prodrugs diffuse easily across the cell membrane by facilitated diffusion and thereby help in improved absorption. It also help in sustained delivery of the parent drug at the site of action for long time. Therefore posterior segment diseases can be managed with therapeutics conjugated with lipid prodrugs.

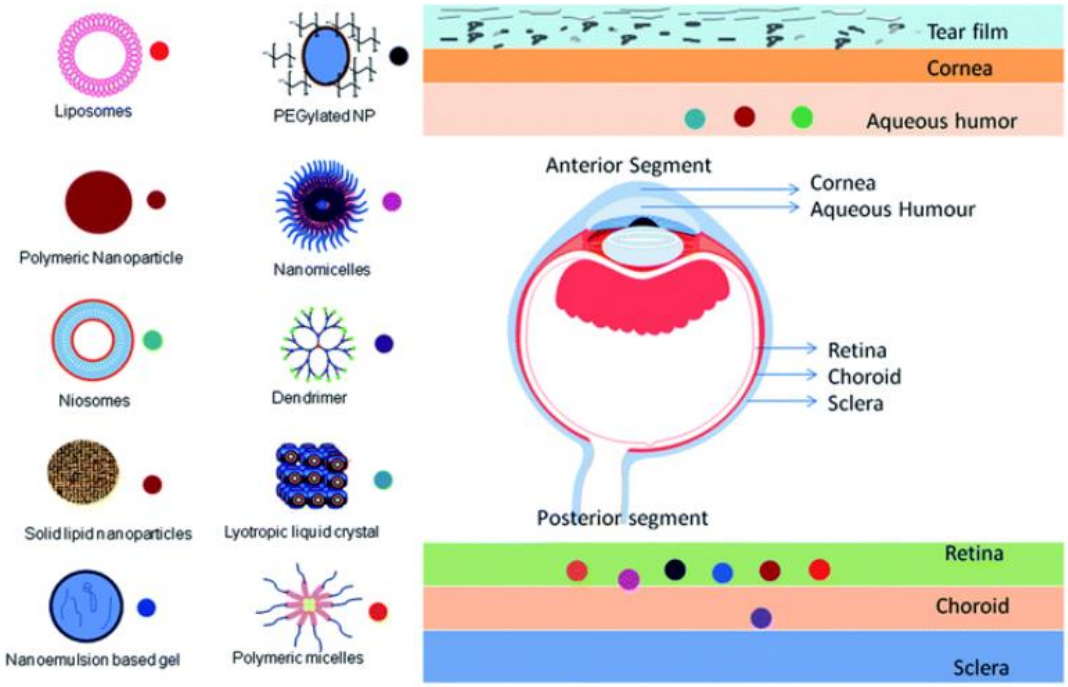
By analysing this statement, the Snehana type of Aschothana is a type of conjugated lipid prodrug. This is really appreciable finding because the science of ayurveda is true since ancient time onwards. Through modern researches we can validate the findings of our acharyas are true and applicable till now.

NANO TECHNOLOGY BASED OCULAR DRUG DELIVERY

Nano technology based system can design size of molecules which can ensure low irritation, adequate bioavailability and ocular tissue compatibility. Several nano carriers like nano particles, nano suspensions,liposomes,and dendrimess have shown promising results for improving ocular drug bioavailability.

Nanocarriers are distinct particulate systems with a particle size in the nanometer range (10–1000 nm) with a specific surface charge. The varying size range provides numerous applications in the area of biomedicine. Various nanocarriers have been explored for their use in ocular applications. Moreover, the surface charge of nanocarriers contributes to their conjugation and retention at the specific site

Figure 4.4.5- different nanocarrier systems and their targeting ability are presented in the following figure



NANOMICELLS

Nanomicells are carriers,commonly used to formulate clear aqueous solution in ophthalmic preparations. Recently nanomicell formulation-based technology for ocular drug delivery have been developed fastly. The reasons may be due to high drug encapsulation capability, ease of preparation, small size, increasing bioavailability of drugs in ocular surface thereby better therapeutic outcomes.

In a study by Civiale et al, developed dexamethasone loaded nanomicelles by employing copolymers of poly hydroxyethyl aspartamide [PHEAC] and pegylated PHEAC(16) for anterior segment delivery. In vivo dexamethasone concentration time profiles were studied and determined in rabbits with aqueous humor sampling. Results showed that dexamethasone loaded PHEA micelles have higher ocular bioavailability relative to dexamethasone suspension. The area under the curve for dexamethasone micellar formulation was 40% higher than that of control suspension. Results suggest that nanomicellar formulations are a viable option for topical ocular delivery of small molecules.(27)

Nanomicellar technology has been found to be very rapidly growing field gaining interest in ocular drug delivery. The reasons may be its small size, hydrophilic corona,

NANOPARTICLES

They are colloidal carriers size ranges from 10-1000nm. For ophthalmic preparations commonly used nanoparticles are lipids, proteins, natural or synthetic polymers such as albumin, sodium alginate, chitosan, poly lactide-co-glycolide (PLGA), polylactic acid (PLA) and polycaprolactone. Drug loaded with nanoparticles can either be nanocapsules or nanospheres. In nanocapsules drug is enclosed inside polymeric shell while in nanospheres it is distributed uniformly through-out the polymeric matrix.(27)

Nanoparticles are best suited as promising candidates for ocular drug delivery because of their small size, owing to low irritation and sustained drug releasing property thus avoiding frequent administration.

As per modern ophthalmic-pharmacokinetics nano particles are best suited with topical application in order to prevent cataract as nanodrug can reach higher lens concentrations where free drug will be washed off easily.

Most commonly used nanoparticles are :

1. Microemulsions
2. Nanosuspensions
3. Nano particles
4. Liposomes
5. Dendrimers
6. Niosomes and discomes

Microemulsions

They are dispersion of oil and water stabilized by surfactants or co surfactants to reduce the interfacial tension. They are thermodynamically stable with a small droplet size and have more permeability to pass the corneal surface. Microemulsions have low surface tension and high spreading coefficient, allowing the drug to spread and mix well with the precorneal fluid. Improved corneal contact time , sustained release effect of drug helped in increasing drug bioavailability and reduced dosing time. So most of the modern ophthalmic drops are now coupled with microemulsions rather than bare liquid forms.

Nanosuspensions

Nano suspensions are colloidal dispersions of poorly water-soluble drugs in a dispersion medium stabilized by surfactants and polymers. Unlike microemulsions they are regarded as ideal because they have less irritation to the ocular surface. Nanosuspensions increase the precorneal residence time and enhance solubility and ocular drug bioavailability.

Nanoparticles

Nanoparticles are colloidal drug carriers with a size ranging from 10 to 1000 nm. Drug-loaded nanoparticles with size ranging from 50 to 400 nm are considered versatile for ocular delivery as they have the ability to overcome physiological barriers and to direct the drug to specific cells, either by passive or ligand mediated targeting mechanismsNano

particles are defined as particles less than 1µm diameter and comprising of various biodegradable and non-biodegradable substances. They can be classified as nanospheres or nanocapsules depending upon whether the drug is uniformly distributed or coated with polymeric substances. Several naturally occurring polymers were identified as carriers for the nanoparticulate system

Liposomes

Composed of one or more phospholipid bilayers with a central aqueous compartment. They have maximum 10µm diameter. Due to central aqueous and peripheral lipid layers they are capable of incorporating both hydrophilic and lipophilic drugs. Liposomes can bind with drugs with low solubility, low partition coefficient, high molecular weight, and poor absorption. Addition to that increased aqueous concentration and bioavailability are the other benefits. The major advancement is that, unlike normal ocular drops that wash away due to tear turnover cationic liposomes (prodrugs charged with positively charged lipids) have more residence time in the cornea. But short shelf- life, limited drug loading capacity and sterilization issues limits the commercial use of liposomes in the market.

Dendrimers

Dendrimers are branched spherical monodispersed polymers. They have specific size shape and molecular mass and can be used as a nano particle in ocular drug delivery as a canvas. They enclose the main drug due to the presence of so many functional groups and covalent bonds. They have unique physical and chemical properties like high water solubility, water encapsulation capability,monodispersity and surface functionalizable groups. The ability to functionalize surface groups make them a suitable candidate for lipophilic and hydrophilic drug delivery.

Niosomes and Discomes

Niosomes are surfactants that are biodegradable, biocompatible, and non-immunogenic they are chemically stable with 10 to 1000 nm in size and are capable of incorporating both hydrophilic and lipophilic drugs. Another novel carrier system is the discome, which is a large structure (12–16 mm) as derived from niosomes by the addition of non-ionic surfactants. Niosomes do not require special handling during preparation and are shown to provide targeted, sustained drug release, and enhanced bioavailability. Discomes have a longer residence time in the cul-de-sac and less systemic drainage due to their large size. Entrapment efficiency of drugs is also higher with discomes than with niosomes.

Table 4.4.1-The comparison of various nano drug delivery system along with their advantage and disadvantage are described as follows.

DRUG DELIVERY SYSTEM	ADVANTAGES	DISADVANTAGES
LIPOSOMES	Bio compatible/ non toxic and improves corneal permeability	Production cost is very high/ encapsulated drug may undergo leakage
NIOSOMES	Less toxic, biodegradable, biocompatible, and mucoadhesive because they are composed of nonionic surfactants	Inefficient drug loading

DIOSOMES	Discomes are giant niosomes (size nearly 20 μm) containing poly-24 ethylene cholesteryl ether, which prevents systemic drainage Disc shape favours discomes fitting into the cul-de-sac, thus improving the drug residence time Self-assembled liquid crystalline nanoparticles with size less than 500 nm Large-scale production is possible	Ineffective drug loading
CUBOSOME	Incorporation of hydrophilic, lipophilic, and amphiphilic therapeutics is feasible with high loading capacity	Exhibits low entrapment efficiency for hydrophilic drugs compared to hydrophobic drug
NANOWAFERS	Effective for the treatment Of corneal neo-vascularization	Inadequate drug loading

DENDRIMERS	Enriches drug solubility and exhibits high drug loading and sustained drug release	Low encapsulation efficiency and storage ability

Cntd..

MICROEMULSIONS	Clear, thermodynamically stable formulations with a droplet size of 100 nm Improves solubility and prolongs release of drug, therefore reducing dosing frequency The presence of a surfactant and co-surfactant enhances the corneal membrane permeability	Stabilization of microdroplets requires large concentration of surfactant and co-surfactant so chances of ocular irritation
NANOSUSPENSIONS	Increases solubility, thus enhancing the bioavailability of ocular drugs Enhances the residence time in the cul-de-sac and prolongs drug release owing to its ability to enhance the inherent solubility of poorly water-	Physical stability, sedimentation

	soluble drugs in lacrimal fluid	
SURFACTANT NANOMICELLS	Enhances the penetration of topically applied ophthalmic drugs through the cornea, thus improving the bioavailability of the administered drug	Ionic surfactants cause toxic effects. Hypersensitivity
POLYMERIC NANOMICELLES	Effective for the delivery of ionic macromolecules Target-specific *i.e.*, selective drug accumulation at the ocular pathological site Cost-effective manufacturing techniques provide high industrial acceptance	Chance of flocculation owing to hydrophobic attractions between the neutral coacervates

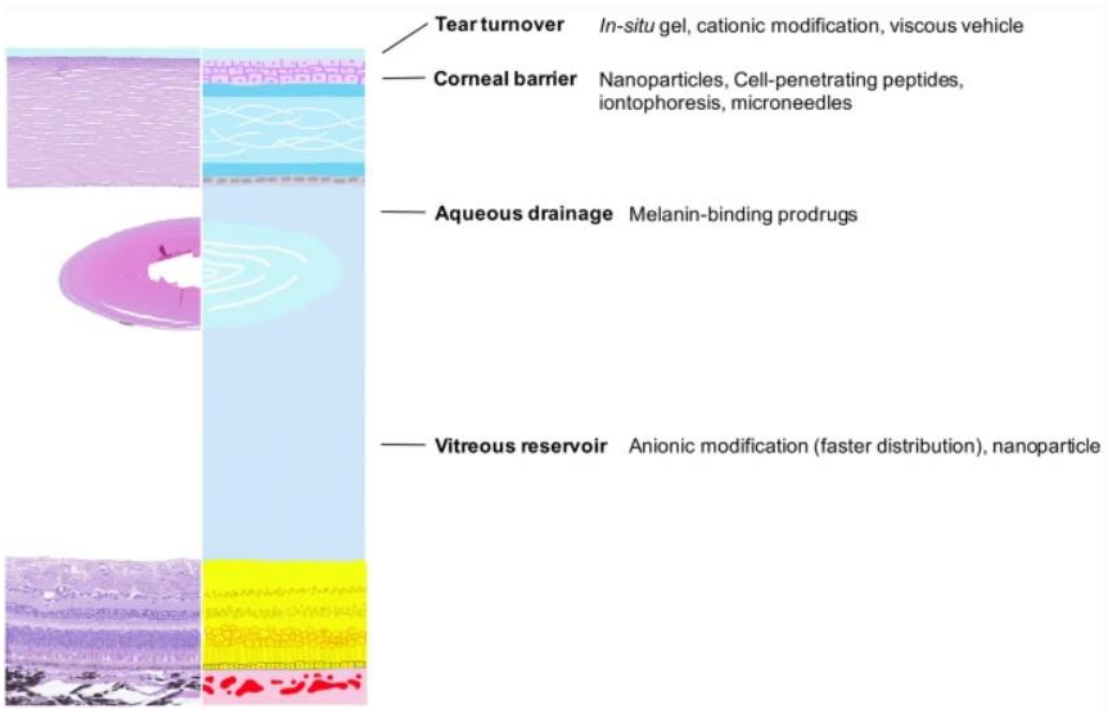


Figure 4.4.6-Schematic drawing of ocular drug barriers and common ways and formulations to bypass these barriers

CONCEPT OF BIO AVAILABILITY IN AYURVEDA(28)

The concept of bio-enhancers or bio-potentiators is new to the modern science. In contrast to this, many drugs as bioavailability enhancers are being used in Ayurveda since time immemorial. The concepts and methods like *Yogavahi, Anupana, Bhaishajya Kala, Bhavana* (trituration), *Rasayana, Yoga* (formulations) and *Kalpanas* (various dosage forms), concept of *Purana Aushadhies* (old drugs), concept of action-augmenting drugs, and penetration enhancers of bio-enhancing are being used since time immemorial in Ayurveda. In addition *Samshodhana* (bio-purification) can also be considered for this concept.

Few among them are

YOGAVAHI

Yogavahi is the pharmacokinetic synergy in Ayurveda means the one that accelerates the properties of others by synergistically combining ingredients for maximum safety and efficacy.(29) It can be considered as drug vehicles when administered with or after the drug work in synergy with the drug to facilitate the action of the drug. Eg; honey, warm water

ANUPANA

The administration of medicament/drug with or after the core drug is known as *Anupana.* Acharya Charaka had mentioned that *Anupana* taken in a proper manner helps in the proper digestion and absorption of drug and food material and ultimately leading to an increased bioavailability.(30) Use of *Anupana* according to *Dosha* is also narrated in classics. For Vata snigdha ushna , for Pitha Madhura seetha and for Kapha rooksha ushna drugs are commonly advised. The concept of *Anupana* basically comes into existence due to the low efficiency of drugs. The co-administration of *Anupana* may increase the bioavailability and efficiency of drugs.

BHAISHAJYA KALA(28)

In Ayurveda, there is description of proper time for administration of medicine in relation to food. Ten *Kala* (times) for administration of medicine in relation to food are mentioned in classics, and these may also help to increase absorption rate of drugs. It include abhaktha/ pragbhaktha/ adhobhaktha/ madhyabhaktha/ antarbhaktha/ sa-bhaktha/ samudga/ muhurmuhu/ sa-grasa/ grasanthara.

BHAVANA

It is a special method for enhancing the bioavailability of drugs. In this, the drug/drugs are triturated with the *Svarasa, Kvatha,* etc., of another drug during the manufacturing of dosage forms to increase the effect of the drug.

Classically, *Bhavana* is used to enhance/modify the potency of a particular single or compound drug. Pharmacologically, these drugs act either by bringing a small change in chemical structure of the principal drug or by increasing the bioavailability of the principal drug, and hence the same doses of the drugs bring about more effective and potent action. Thus, the process of *Bhavana* should logically be considered as an important measure for enhancing bioavailability.

BIO AVAILABILITY ENHANCERS IN TOPICAL APPLICATION OF EYE

Use of herbal extracts to treat ophthalmic conditions dates back to ancient times. The ocular drug delivery is in a transition from empirical to rational base. This is because of better understanding of anatomical as well as histological aspects of ocular tissue and also development of so many animal models for research practices. Despite technological innovation that allows the synthesis of new drugs, biologically-active molecules extracted from plants and animal tissues continue to stimulate extensive research and investment. However, many of these naturally-occurring compounds have yet to be rigorously investigated for activity in ocular tissues.

Use of naturally occurring as well synthetic polymers from natural products are the areas of active research in order to increase the bioavailability of the products.

Research into compounds from a variety of flora and fauna that might serve as drug prototypes for treatment or prevention of various ophthalmic diseases are available in research articles like aloe vera , curcumin, caffeine, xantjophills, carotenoids, hyalouronic acid, linum usittassimum etc can be used.

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THE SYNTHETIC POLYMERS FROM NATURAL PRODUCTS INCLUDE :

VISCOSITY MODIFIERS- modification in viscosity is necessary to increase the residence time of topical applications. The most commonly used viscosity polymers are cellulose, polyvinyl alcohol, and poly acrylic acid. Polysaccharides such as xanthan gum were found to increase the viscosity and delay the clearance of the instilled solution by tear flow. Herbal drugs of various solubility incorporated into these polymers to form gels.

MUCOADHESIVE POLYMERS- are the type of polymers get attached to the mucin layer of tear film secreted by the goblet cells in the cornea. They remain attached to mucin and remain in the vicinity of mucin as long as it is present and referred to as mucoadhesive polymers.

POLYACRYLIC ACID- Carbopol- cross linked polyacrylic acid have excellent mucoadhesive properties causing significant improvement in bioavailability.

Caboxy-methyl-cellulose is found to be an excellent mucoadhesive polymer.

IN SITU GELLING SYSTEM- In early eighty's concept of in situ gelling come existence these systems will have low viscosity and will be instilled as eye drops and will change in to gel like system when in contact with corneal fluid. This sol to gel transition can be brought about by three ways. Change in temperature, change in pH and ion activation

COLLOIDAL SYSTEMS

Colloidal carriers like liposomes nano particles found to be useful to prolong the corneal contact time and hence more and more tested in ocular drug delivery. Nanoparticles are polymeric colloidal particles ranging in size from 10-100nm. Various polymers like poly-acrylamide, polymethyl-meth-acrylate, albumin gelatin, poly-alkyl-cynoacrylate, polylactic-co-glycolic acid, ε-caprolactone used in the preparation of nanoparticles.

CHAPTER FIVE

CRITICAL ANALYSIS OF KRIYAKALPA WITH SPECIAL EMPHASIZE ON ASCHOTHANA

According to Ayurveda , chikitsa can be divided into three ways- *antha:parimarjana, bahiparimarjana* and *sasthrapranidhana*. Antha parimarjana is the purificatory procedures that eliminate or subside the morbid matters from the body and bahi parimarjana means application of medicines externally. Sasthra pranidhana include various kinds of surgical procedures.(31) Kriyakalpa belongs to the group of bahi parimaarjana chikitsa.

The word Kriyakalpa is composed of two words- kriya and kalpa.

Kriya is formed by kri plus sa prathyaya . The variants of which are arambha, shiksha, nishkriti, pujana, sampradharana. *Kriya* refers to the various procedures that are undertaken or carried out.

Dalhana, while commenting about Kriyakalpa adhyaya it is mentioned that '*kriyanam tarpanaputapakadinam kalpanam karanam kriyaakalpa:'*it is the unique branch of medicine that deals with specialized topical ocular procedures along with their preparations for the management of various ophthalmic conditions. It is a practical/ feasible/ proper or competent method where medications are applied locally around the eyes.Attainment of an effective concentration of medicine for a stipulated period of time is the main objective of these therapies.

Searching answer to the question why Kriyakalpa got more popularity, we can assume many factors like ease in application, cost effectiveness, preventive and curative effects are the main. In addition to that ocular surface have direct contact with outer environment so topical applications have more priority than oral application in case of Nethra roga.

All the Kriyakalpa were written in the ancient time period. Even without using much sophisticated instruments development specific methodology was possible, and are applicable in this modern era too.

CLASSIFICATION OF KRIYAKALPA

Kriyakalpas have been classified according to the stage, severity and site of disease. Different acharyas classified Kriyakalpa on the basis of their own views and concepts

Charaka samhitha

Acharya charaka popular in chikitsa delas with diseases of the entire body without paying any special reference to disorders of salakyathanthra. However, some references are available regarding the eye ailments saying that eye disorders should be treated with the help of *Anjana, Ashchyotana, Vidalaka* and *Tarpana*.(32) No further details are available with *Charaka*, in reference to *Kriyakalpa.*

Susrutha samhitha (33)

According to acharya susrutha Kriyakalpas are 5 in number.

Tarpana, putapaka, Aschothana parisheka and Anjana

Vagbhata (34)

According to vagbhata of ashtanga samgraha Kriyakalpas are 6 in number- Aschothana, parisheka, bidalaka, Anjana, tharpana and putapaka.

Sarngadhara samhtiha (35)

While mentioning various kalpanas acharya sjarngadhara has classified Kriyakalpa into 7

1)Tarpana
2) *Putapaka*
3) *Ashchyotana*
4) *Parisheka*
5) *Anjana*
6) *Pindi*
7) *Bidalaka*

Table-4.5.1Different types of Kriyakalpas according to Ayurvedic claassics

KRIYAKALPA	*CARAKA*	*SUSRUTHA*	*VAGBHATA*	*SA*	*BP*
SEKA	-	+	+	+	+
ASCHOTHANA	+	+	+	+	+
ANJANA	+	+	+	+	+
THARPANA	+	+	+	+	+
PUTAPAKA	-	+	+	+	+
PINDI	-	-	-	+	+
VIDALAKA	-	-	+	+	+

Aschothana is the way of instillation of the drug in the form of drops into the eyes from a height of 2 Angulas. It is the preliminary method of all ophthalmic medication employed in all eye diseases. Charaka acharya mentioned three Kriyakalpas in chikitsa sthana- vidalaka/ Aschothana and Anjana.

Indications of Aschothana – according to acharya Susrutha Aschothana is indicated when the dosha vitiation is minimal.(36) According to Vagbhata Acharya Aschothana can be done at the beginning itself in suitable cases. As already mentioned in the chapter of Kriyakalpa , Aschothana helps to alleviate pain/ itching/ grittiness/ redness and foreign body sensation

Contra indication – Aschothana is prohibited in night and when the dosha is vitiation is more

ANALYSIS OF METHODOLOGY OF ASCHOTHANA

POORVA KARMA

Positioning of patient: - The patient is lying in supine position. In order to avoid irritation of ocular surface a room devoid of wind/ dust/ excessive light is insisted in classical literature. The supine position of the patient helps to increase the adherence of medicine in ocular surface when compared to sitting or standing position.

PRADHANA KARMA (37)

It is the procedure of instillation of specified drops of liquid medicine to the eyes kept open from a height of two Angulas. The drops are allowed fall from a pichu varthi hanging from a sukthi over the *Kaneenaka sandhi* i.e. inner canthus. This allow to increase the retention time of medicine over the eyes as well as prevent the rate of reflex blinking and watering. As per modern research articles eye drop instillation in the medial canthus seems to be an effective means of ophthalmic drug delivery compared to conventional ways.

But as per sarngadhara acharya site of application of medicine is drik Madhya

DHARANA KALA – 100 vakmathra is said to be the retaining time of Aschothana as per our classical reference (36)

Table 4.5.2-SAMYAK LAKSHANA (38)

Prasanns varna, visada	Clarity of vision
Vata atapa saha	Free from irritations of ocular surface
Laghutva	Lightness of eyes
Sukhaswapna prabodhana	proper sleep

MODE OF ACTION

According to vagbhata acharya, the instilled medicine penetrate into the *sandhi* (conjunctival fornix, medial Canthus) reach the naso lacrimal drainage pathway (*ghrana mukha srotamsi)*and help to eliminate the vitiated dosas from *jathrurdhva*.

As described in the perspective of nasya karma pathway of nasal medication through sringataka marma, reaching the junction of *Nethra-srothra-ghrana-mukha* & perform either virechana/ samana or brimhana karma as per the drugs used. Similarily Aschothana medication is passing through the nose, get absorbed by – simple diffusion into nasal mucosa/ absorbed through capillaries / may pass through olfactory pathway and reaches limbic system and hypothalamus. The role of topical applications in acute and emergency conditions like treatment of poisioning/ syncope/ coma/ CNS related conditions are already described by our acharyas in a very detailed way. References regarding action of Aschothana emphasizing these points.

ATHIYOGA LAKSHANA- The Lakshanas of excessively performed Aschotana includes *Ruja* (pain in the eyes), Sopha (swelling of eyes), *Pidika* (blisters in the eyes), *Timira* (reduct,ion in eye sight) (33)

AYOGA LAKSHANA - Hinayoga of Aschyotana leads to *Paka* (pus formation in the eyes), *Asru* (excessive tear secretion in the eyes), *Harsha*, and *Doshodgama* (vitiation of all doshas). The Pratikriya for Atiyoga and Hinayoga of Aschyotana includes performing appropriate Doshahara measures like *Dhumapana, Nasyakarma and Anjana*(36)

ANALYSIS OF DIFFERENT TYPES OF ASCHOTHANA

According to classics there are three types of Aschothana- viz Snehana/ Ropana and Lekhana according to vata/pitha and kapha predominance. The doses of these three kinds of Aschothana along with drug properties are summarized as :

Table 4.5.3- Doses three kinds of Aschothana along with properties of drugs used

Karma	Dosha	Dosage – in drops	Drug properties	Time of Aschothana
Snehana	Vata	10	Thiktha, snigdha	Evening
Ropana	Pitha	12	Madhura, seetha	Afternoon
Lekhana	Kapha	8	Thiktha,ushna, rooksha	Morning

Ayurvedic literature is enriched with different kinds of examples for the three kinds of Aschothana Kriyakalpa. Use of herbal drugs in the form of eyedrops were followed in Kerala as a part of traditional medicine.

Description about Aschothana can be taken up from the following texts :

- Caraka samhitha
- Ashtanga Hridaya
- Ashtanga samgraha
- Susrutha samhitha
- Sarngadhara samhitha
- Chakra datta
- Bhaishajya ratnavali
- Yogamrutham
- Chikitsa manjari
- Sarvaroga chikitsa nool
- Sahasrayogam

Traditional use of herbal eyedrops for various aliments were described in different classical literature written centuries back

Caraka samhitha is one of the oldest textbook in Ayurveda, written by Agnivesa and redacted by Acharya Caraka. All aspects about health, disease and chikitsa were described in it. In soothrasthana (chapter ?) single drug therapy is mentioned for different diseases. For Nethra roga, thriphala is advised.

Sloka with ref citation

Benefits of thriphala according to acharya Vagbhata include – best known rejuvenate with action against skin and eye diseases, helps to pacify kleda,meda,prameha and kapha raktha vikaras.

According to sarngadhara thriphala Aschothana is said to be thridoshahara. (ref cit)

Practically thriphala is converted in the form of arka & used as Aschothana.

Benefits of thriphala in Nethra roga chikitsa is very vast. It is a very potential drug reported in ayurvedic literature with antimicrobial, immunomodulatory, anti- diabetic and anti-mutagenic activity. Scientific exploration of thriphala have shown that ethyl acetate and acetone extracts of triphala have better bactericidal and antioxidant property. These extracts were characterized with antimicrobial property against microbes causing eye infections.(39)

Nethra roga chikitsa described by Acharya Vagbhata in uthara thanthra of Ashtanga hridaya contain descriptions about Aschothana Kriyakalpa as follows :

Table 4.5.4 Different examples of Aschothana according to Ashtanga Hridaya

DISEASE	DOSHA	Aschothana
Upanaha	Kaphaja	Patola pathra amalaka kwadha
Arjuna	Raktaja	Sarkara, mastu, kshoudra
Abhishyanda	Vata	Bilwadi panchamoola, eranda, jadamanchi, brihati, madhusigru Kashaya
Soola in abhishyanda	Vata	Hribera tvak, sarngeshta, udumbara tvak with aaja paya
Abhishyanda	-	Darvi prapoundarika kvadha
Abhishyanda	Kaphaja	Nagara, thriphala, nimba, vasa and rodhra Kashaya
Abhishyanda	Pitha raktha	Swetha rodhra, madhuka, in powdered form mixed with breast milk

According to Vagbhata mainly kashaya/ ksheera Kashaya/ breast milk along with medicines as per dosha predominance are used.

Table 4.5.5 Aschothana Yogas according to Acharya Susrutha

DISEASE	DOSHA	Aschothana
Abhishyanda	Vatika	Saindhava/ udeechya/ yashti/ pippali in the form of ksheera Kashaya
Abhishyanda soola	Vatika	Hribera/ vakra/ manjishta/ udumbara tvak in the form of ksheera Kashaya made of aja ksheera
Abhishyanda	Paithika	• Samudraphena with honey and breast milk • Yashti/ lodhra/ draksha/ sarkara/ utpala with breast milk • Yashti / sarpi and lodhra • Kasmari/ dhathri/ pathysa with water • Katphala in water
Abhishyanda	Kaphaja	Rooksha ascothana
Abhishyanda	Rakthaja	Snigdha Aschothana

Susrutha acharya mentioned all the three types of Aschothana according to doshik status. Especially Ropana Aschothana is mentioned for paithika abhishyanda and mainly breast milk is used as the medium. Stanya or breast milk have properties like Madhur Rasa (sweet), KashayaAnurasa, Sheeta, Laghu, Pathya, Jeevaniya, Brmhaniya (anabolic), Deepaniya (digestive), and Satmya (favourable/wholesome)(40)

Modern research field studied non nutritional use of breast milk. The bioactive agents which comprise human milk are capable of inhibiting inflammatory processes, as well as increasing the production of specific antibodies, antioxidants, interleukins, growth factors, secretory leukocytes, and defensins. Oligosaccharides contained in human milk limited adhesion of pathogens to conjunctival epithelium and intestinal mucosa. (41)

References regarding traditional use of herbal medicines in the form of eyedrops for managing conditions like acute infections/ foreign body affection/ redness/ itching and watering are available in ayurvedic compendiums of Kerala like Yogamrutha, Chikitsa manjari, Sahasrayoga and Sarvaroga chikitsa nool. Plants available at the rural areas are used as swarasa in the medium of breast milk or plain water. All these references can be considered as a proof that the use of herbal drugs in the form of eyedrops were in use since ancient time onwards.

Table 4.5.6-The most common plants with their indication according to Traditional Text books of Ayurveda:

DRUG	INDICATION	MEDICINAL FORM
Drone pushpin/ Leucas cephalotes (BN)/ Thumba (Malayalam)	Neonatal eye infections	Drone pushpin swarasa with saindhava lavana
Poovam kurunthil (Malayalam) / Iron weed (English)	Neonatal eye infections	Swarasa with breast milk
Sigru pallava or tender leaves of drum stick with sandal wood	Neonatal eye infections	Along with breast milk
Crepe jasmine (English name)/ Nandiyarvattom (Malayalam)	Congestion of eyes	Latex of young flower buds/ flower juice along with breast milk/
Amalaki/ Goose berries (English)	Pain of eyes	Along with breast milk
Alteranthera glabra (BN) Ponnangaanni or kozhuppacheera (Malayalam) with butter	Pain, watering, discharge, redness of eyes	Leave juice with butter

Management of viral conjunctivitis with herbal eyedrops were mentioned in Yogamrutha as a separate section. Different kinds of Lekhana and Ropana yogas for alleviating redness, itching watering and discharge of eyes were described. (42)

The main ones among them include :

1. Leave juices of iron weed or Poovamkurunthil i(n Malayalam) along with as such or after adding with breast milk.
2. Daruharidra Kashaya along with honey

3. Pippali and kathaka along with breast milk
4. Apamarga swarasa in the medium of rice water

Research articles regarding use of medicinal plants and natural products have shown an ethnopharmacological and ethnobotanical data regarding around 44 raw drugs in the form of eyedrops were in use since ancient time onwards whole over the world. All these can be considered as a proof that traditional practice of Aschothana was existed in India as well as some foreign countries.

CHAPTER SIX

EXOPHTHALMOMETRY

Exophthalmometry is the assessment of the anteroposterior position of the globe in the orbit relative to the orbital rim. Though a number of orbital diseases may be evaluated based on the degree of exophthalmos, there is still no gold standard method for the measurement of this parameter.

One of the most widely used methods is Hertel exophthalmometry (HE). It is a simple easy technique in determining proptosis or anterior protrusion of eyeball. It is a quantitative technique to determine the position of eyeball to orbital space. Knowledge of normal exophthalmometric values have a great role in understanding various pathological conditions of eye and orbit.

Exophthalmometry helps to get anteroposterior measurement of globe in the orbit. The orbital space contains eyeball, extra ocular muscles, retro-orbital fatty tissue and orbital vasculature. Total volume of eyeball is 30 ml. Exophthalmometric measurement is taken from lateral orbital rim to the apex of cornea. Various exophthalmometers are available among them, Hertel and Leudde types are commonly used. Ocular protrusion show variability according to ethnic changes, refractive status of the eyes, axial length, age, gender, height weight, BMI. The normal range of protrusion in humans are accepted as 12-21 mm(43).

Ethnic variations can cause changes in the physical constitution and shape of the face. Aging may cause atrophy of retro orbital fatty tissues. High myopia can cause pseudo protrusion and this shows axial length is very much closely related to exophthalmometric measurements. In a study conducted to find out the role of age, gender, refractive status and axial length on the Hertel exophthalmometry, values showed every 4mm rise in AL cause 1 mm rise in hertel exophthalmometric values. Wide individual variation in the facial skeleton is the main cause of variation in the values(43).

A study was conducted to establish a set of exophthalmometric values in a normal Indian population and to compute a regression equation for calculating these values. . Hertel's exophthalmometer was used to measure the degree of protrusion of the eyes.

Statistical methods were used to calculate the mean values in the right and left eye in either sex and to compute a regression equation for calculating the exophthalmometric values. The range of exophthalmometric values in a normal Indian population aged 3-80 years was 7-19 mm for males and 7-21 mm for females. The exophthalmometric values were higher in the first decade, decreased in the second decade, and increased again in the third decade. They then remained stable for the next three to four decades. The peak was reached in the seventh decade in males and in the sixth decade in females. The lowest values in both sexes were attained in the eighth decade. The regression equations for the calculation of the exophthalmometric values are: In males for the right eye: Exophthalmometric value = 12.43 + 0.25 x age; In males for the left eye: Exophthalmometric value = 12.30 + 0.029 x age; In females for the right eye: Exophthalmometric value = 13.30 - 0.003 x age; In females for the left eye: Exophthalmometric value = 13.17 - 0.0003 x age.(44)

The quantitative measurement of position of globe in the orbit is very important clinical parameter. Although the normal limits of protrusion of the human eye are accepted to be between 10 and 21mm, exophthalmometric values have been shown to vary with ethnicity, age, gender, height, weight, body mass index (BMI), orbital parameters, refraction and axial length (AL) of the eye.(45)

CHAPTER SEVEN

CONCEPT OF PRAKRITHI

The substratum of ayurvedic theories depended on basic theories like THRIDOSHA SIDHANTHA & PANCHAMAHABHOOTHA SIDHANTHA. According to Ayurvedic parlance every creation in this earth are under the influence of thridosha and pancha mahabhootha. The equilibrium of all these can be considered as prakrithi and derangement of them leads to vikrithi or vikara (disease). According to Aruna Datta prakrithi is sareera Swaroopa. So it can be considered as the enumeration of body features both internal and external.(46)

Prakrithi is one of the basic denominator in ayurveda which defines the physical/ physiological and psychological traits of an individual.(47) The prakriti determined at the time of conception depend on various factors involving metaphysical (aatma, purvajanma-krita karma), psychological (sattvaja), protophysical (five classical elements), hereditary (matraja, pitraja), maternal diet, lifestyle, doshik dominance in the maternal reproductive tract, place of birth, time of birth, age of parents, socio-economic condition, and idiosyncrasy.

Thus prakrithi can be defined as the equilibrium of three dosha and is considered as healthy. Some may have predominance of any one dosha also. Such single dosha predominance is considered as sick. (48)

The humors combine among them in seven types of constituents. They are *vata, pitta, kapha, vata-pitta, vata-kapha, pitta-kapha,* and *vata-pitta-kaph.(thridoshaja*) This basic constitution which is fixed at the time of fertilization generally remains constant through out the life of that individual.(49)

The prakriti determination in Ayurveda is very important in the context of practice of traditional medicine and for its application in diagnostics, disease management, and prognostication of a disease or a condition. Traditionally, the prakriti assessment is carried

out by the ayurvedic physician on the basis of his knowledge and experience and is therefore subject to inter-observer variations.

Assessment of prakrithi help to understand the mental and physical nature of a person and also helps to know the susceptibility to diseases which assists in promotion of health, prevention and cure of diseases.

As per classical references we can find out the characteristic features of each prakrithi purusha in various contexts. Depending upon prakrithi shape and nature of eye may vary from person to person. This is important while doing Aschothana because

CHAPTER EIGHT

STANDARDIZATION

International Standard Organization (ISO) defines standardization as "the process of formulating and applying rules for an orderly approach to a specific activity for the benefit and with the co-operation of all concerned, in particular for the promotion of optimum overall economy taking due account of functional conditions and safety requirements (American National Standard Institute:2002)." Standardization determines not only the basis for the present but also for future development and it should keep pace with progress. Standard is the result of a particular standardization effort, approved by a recognized authority.

According to WHO guidelines, standardization is a measurement for ensuring quality and is used to describe all measures which are taken during the manufacturing process and quality control leading to a reproducible quality.

Process standardization can be defined as the improvement of operational performance, cost reduction through decreased process errors, facilitation of communication, profiting from expert knowledge (Wüllenweber, Beimborn, .Weitzel, & König, 2008, p. 212), and providing flexibility without sacrificing organizational controls (Røhnebæk, 2012).

Standardization of any procedure needs some criteria like

1. Recognition of the need for standards in a particular area.
2. Clear definition of the scope and purpose of the standard.
3. Review of existing standards in order to determine whether or not they meet the needs (even with minor modifications or selection of options)
4. Widespread review and pilot implementations of the draft standard to resolve ambiguities, imprecise requirements, and incomplete functionality.

STANDARDIZATION IN AYURVEDIC MEDICINE

Generally, all medicines and medical procedures need to be standardized in order to ensure safety and efficacy. The modern system of medicine is based on sound experimental data, toxicity studies, and human clinical studies. Ayurveda is a science of life with a holistic approach to health and personalized medicine. It is one of the oldest medical systems, which comprises thousands of medical concepts and hypotheses. Ayurvedic treatment is highly effective; but the proper mode of action, pharmacology, pharmacokinetics, and pharmacovigilance, of many important drugs as well as the standardized practice of many therapeutic procedures like pancha karma procedures, Nethra Kriyakalpas need scientific validation and a general protocol because these procedures have great influence in complete management of the disease.

Aschothana is the method of application of decoctions/juices of herbal raw drugs/ and medicated lipids for a preset duration of time. Among topical applications, Aschothana is a simple, effective & patient-friendly procedure having an important role from ancient times onwards. The method of application and dose of this Kriyakalpa are the two important fields to be discussed well because of mismatching findings of conjunctival holding capacity, size of one drop with that of ayurvedic classical references.

Standardization studies regarding dose in the ayurvedic research field have occurred in the context of Nasya karma. From that study, Bindu is the unit of measurement explained for the dose of Nasya. In routine Ayurvedic practice, one Bindu is considered as one drop (0.05ml), but according to the definition of Bindu and standardized quantity mentioned by Acharyas, it is 1 Shana (sarngadhara) which is ten times more than the routinely practiced dose.

90 volunteers aged between 16 to 60 years were considered, 30 in each group (3 groups total), irrespective of sex and age were selected for the study. The liquid selected was tila taila and in the first group drops dripped from anguli (32drops) is measured. In the second and third group, drops from the dropper and in the third group measured the Bindu of Tila Taila explained by Acharya Hemadri.

From the study, it is observed that

- Dose for Nasya differs if one goes with the textual method than the routinely prescribed method.
- Bindu is not equivalent to drop.
- Routinely practiced dose is 10 times lesser when compared to classical dose.
- Measurement of Bindu should be defined in milliliters in standard literature or in the Formulary so as to avoid the misinterpretation of the quantity of Bindu.
- The quantity of one Bindu by Bindu method is approximately 0.44 ml (14.34 / 32Bindu)

INTERPRETATION OF DIFFERENT CONTEXTS OF BINDU PRAMANA(50)

Definition of Bindu – explained in the context of nasya

Bindu is defined as the total quantity of collected liquid medicine (Sneha, Swarasa, Kashaya, etc.) that dribbles down when the first two digits of the index finger (proximal and middle phalanges) are dipped into it and taken out of the same.

From this definition, it is clear that the quantity of bindu varies from person to person as the size of anguli changes. The quantity of Bindu also varies according to the Drava dravya used for the Nasya. It would be practically convenient if a standard or fixed quantity of one Bindu can be decided for any of the Drava dravya used for Nasya. Such an attempt of Standardization of Bindu for Nasya was at first successfully done by Acharya Sharangadhara in 14th century.

As per sarngadhara, Bindu is equal to one Shana and further, the dose of Marsa Nasya is explained in multiples of Shana itself, as 8 Shana, 4 Shana, and 2 Shana for Pradhaana, Madhyama and Heena Maatra.

According to Sharangdhara 1 Shana = 4 Maasha.

4 Maasha = 4 gm = 4ml (Ayurvedic Formulary of India).

Thus, 8 Bindu = 1 Shana = 4 ml. 1 Bindu = 0.5 ml.

According to the Ayurvedic Formulary of India, 1 drop = 0.05ml. 10 drops = 0.5 ml.

It can be stated from the above explanation that the standardized quantity of one Bindu for Nasya is 0.5 ml (10 drops).

Bindu in the context of Aschothana

The dose of Aschothana is stated as 8-10-12 bindus for Lekhana Snehana and Ropana types. The Bindu in this context is determined by the drops falling from a Pichu varthi hanging from a sukthi. Here also the quantity of bindu varies on changing the liquid medium, the material used for making varthi, and the size of the varthi. Unlike nasya Bindu in the context of Aschothana is didn't standardize yet. All the practitioners consider the drop size as .05 ml & the method of using Pichu varthi is not followed by all in order to keep a sterile environment. As per modern research articles, size of conjunctival capacity is 30 µl and the size of one single drop is .05 ml. thus accommodation of even one drop of a solution is still doubtful & prescribing a dose of 8-10-12 bindu is not at all practical. Because the medicine will overflow and bioavailability gets reduced. Some scholars consider these 8-10-12 drops as the maximum doses and for one-time use, 2 drops are enough. But these findings can not be accepted completely. The reasons are :

1. In the context of nasya itself it is proven that one drop is not equal to one Bindu.
2. The Bindu in the context of Nasya can not be taken for Aschothana. Because here Bindu is the quantity falling from a Pichu varthi hanging from a sukthi.
3. The quantity is dependent on the size and material of Pichu varthi, & the characteristics of the liquid used.
4. The liquid holding capacity of the eye varies from person to person due to changes in values of exophthalmic measurements, size and shape of eye.

RELEVANCE

RELEVANCE OF THE STUDY

RATIONALE OF STUDY

Aschothana is a simple and patient-friendly procedure, but doses of the three kinds of Aschothana are confusing due to the fact that conjunctival capacity is very less compared to the size of one drop of medicine. Research studies regarding this area of Aschothana are not yet covered up. Hence standardization of the dose of Aschothana is found to be important

RELEVANCE OF THE STUDY

Compared to allopathic medication ayurvedic management of ophthalmic diseases is having special therapeutic procedures known as Kriyakalpa. Aschothana is one among the different types of Kriyakalpa where medicated drops of medicine are instilled into eyes from a height of 2A. Traditional medicine particularly herbal medicine is considered as one of the major healthcare provider around the globe particularly in rural and remote areas. While comparing the dose of Aschothana with modern eyedrops the latter is very big. According to modern pharmacology, the conjunctival sac cannot accommodate even one drop of medicine, so prescribing Aschothana in the classical method is a difficult task.

The traditional practice of Ayurveda has proven that Aschothana is a simple procedure where some persons allow the medicine to stay within the eye for the specified duration of time while some persons practiced it as an eyewash method where medicated drops are allowed to spill out of the eyes. But nowadays practice of Aschothana is similar to instilling modern ophthalmic drops. Without considering dosha all practitioners are prescribing Aschothana up to a maximum dose of 3 drops. But with due consideration of certain factors possibility of accommodating classical dose can be checked. So far, studies regarding this aspect of Aschothana didn't happen yet. Therefore through this study efforts have been made to standardize the dose of Aschothana.

METHODOLOGY

METHODOLOGY

Title of the study :

Standardization of dose of Aschothana procedure

Objectives of the study :

1. To find out the maximum dose of Bindu that can be accommodated in the eye for various types of Aschothana like Snehana, Ropana and Lekhana
2. To determine the various factors influencing the dose of Aschothana

MATERIALS AND METHODS :

Hypothesis

Null Hypothesis :

It is not possible to standardize the dose of Aschothana

Alternate Hypothesis :

It is possible to standardize the dose of Aschothana

Methodology

A. Trial design :

1. Conjunctival capacity is tested in 60 healthy volunteers selected randomly.
2. For standardizing the dose of Aschothana 30 diseased persons indicated for Snehana Lekhana and Ropana Aschothana are selected from OPD of Salakya tantra Government Ayurveda College, Puthiyakavu. Outcomes are assessed on the same day itself.

3. Standardization of Pichu varthi is done using different materials like gauze/ cotton/ kora cloth and cotton cloth
4. Different sizes of varthis are also tested

B. Setting: Department of Salakya tantra, Govt. Ayurveda College Tripunithura,Eranakulam

C. **Sample size:** 90

D. Sampling technique: Convenience Sampling

E. Selection of the patient: As per inclusion and exclusion criteria

DATA COLLECTION

Primary data were collected using the pilot study, and literary research.

DIAGNOSTIC CRITERIA

No specific diagnostic criteria are developed as a part of the study. The aim of the study is to do standardization of dose rather than checking the effectiveness of Aschothana. So diagnosed cases from OPD /IPD are selected for standardizing the dose

SUBJECTIVE CRITERIA

- Patients having no ocular or systemic illness are selected for testing conjunctival capacity using sterile water.
- For standardization of Aschothana dose, OPD /IPD patients requiring Snehana Ropana and Lekhana Aschothana are selected after necessary clinical examinations

OBJECTIVE CRITERIA

1. Visual acuity
2. Schimmer's test
3. Fundus examination
4. Slit-lamp examination
5. Necessary hematological examinations

All these tests were done in order to rule out the conditions as per exclusion criteria like emergency conditions/ surface disorders/ pterygium,

SUBJECT INCLUSION CRITERIA

- Healthy volunteers &patients of the age group 18 years onwards are selected randomly
- The diagnosed ocular cases require Snehana, Lekhana, Ropana Aschothanas from OPD of Salakya tantra Govt.Ayurveda College Tripunithura

SUBJECT EXCLUSION CRITERIA

- Patients suffering from severe pain, redness, and other acute inflammatory conditions require emergency management.
- Patients having any surface disorders of the eye/growth like pterygium

INTERVENTION PROCEDURE

STANDARDIZATION OF PICHU VARTHI

Prior to the standardization of the dose of Aschothana standardization of Pichu varthi is important.

The number of drops coming from Pichu varthi is supposed to be dependent on factors like

- ❖ The material used for making varthi
- ❖ Size of varthi (L*B)

The material used for making varthi

- Different kinds of materials are used like cotton/ kora cloth/ cotton cloth/ gauze piece
- 5 ml sterile water is taken in a sukthi or gokarna
- Pichu made up of each of these materials in a length of 10 cm * 5 cm are dipped in the sukthi.
- The time is set for 2 minutes.
- Water is allowed to flow drop by drop into another empty bowl
- During the two minutes of time, flow of water is observed.
- From that, ideal varthi is the one having calculated dose as per classical references are possible can be fixed for doing Aschothana

Size of varthi

- The maximum length of Pichu varthi is fixed as the maximum that can be included in the sukthi filled with medicine which is 10 cm (7 cm is the length of sukthi and 3.52 cm for two angula heights, which can be totally rounded to 10 cm)
- Different breadths are taken Maximum is taken equal to that of length
- Sukthi is filled with 5 ml sterile water.
- Time is fixed as 2 minutes
- Different sized varthis are dipped in sukthi and no of drops falling out is measured and counted.
- Ideal varthi is selected as the one with which calculated dose as per classics is possible.

COMPARISON OF PICHU VARTHI AND EYEDROPPER BOTTLE

- A comparison of dropper bottle method with Pichu varthi should be done because using Pichu varthi is not possible in all situations. The chance of contamination is very less in the eyedropper bottle method compared to the other.
- Different kinds of media are selected and 30 drops are allowed to fall over a clean empty bowl using Pichu varthi and eyedropper bottle
- The quantity of medicine that is fell down is measured using a micro-pipette

CALCULATION OF AMOUNT OF DROPS THAT CAN BE HELD IN THE EYE – USING STERILE WATER

- 60 healthy volunteers are selected randomly having no ocular or systemic illness
- Case proforma is filled and visual acuity is checked.
- The volunteer is instructed about the procedure
- Using an exophthalmometer measurement is taken and noted
- Using sterile water liquid holding capacity of the eye is measured in drops, at drik Madhya and kaneenaka sandhi

DOING ASCHOTHANA IN LEKHANA SNEHANA AND ROPANA IN INDICATED PATIENTS.

- Case proforma is filled and necessary investigations are carried out
- Required type of Aschothana is selected -mainly Mridweekadi arka is used as Ropana Aschothana, Honey as Lekhana Aschothana dravya, and Durva ghritha as Snehana Aschothana in this study
- Exophthalmometric measurements are taken
- Aschothana is done at Drik Madhya and Kaneenaka Sandhi
- The numberer of drops that can be held in the eyes is noted and recorded

ASSESSMENT

Assessment can be recorded on the same day itself.

Contact with the patient should be maintained till the 7^{th} day for any side effects

ANALYSIS OF OUTCOME

STATISTICAL ANALYSIS

The data of patients were collected on the basis of observations which were further subjected to statistical analysis. A chi-square test, is a statistical test used to compare observed results with expected results. The relation between variables is tested using the Pearson correlation formula. The purpose of this test is to determine if a difference between observed data and expected data is due to chance, or if it is due to a relationship between the variables under study.

The obtained interpretations were

- Insignificant $p>0.05$
- Significant $p<0.05$
- Highly Significant $p<0.0001$

RESULTS

RESULTS

In this section, for the further analysis of the collected data, the gathered details are formulated into tables and graphs. The data collected were categorized into the following headings.

Section A: Statistical analysis of the Demographic Data
Section B: Data associated with the response to procedure

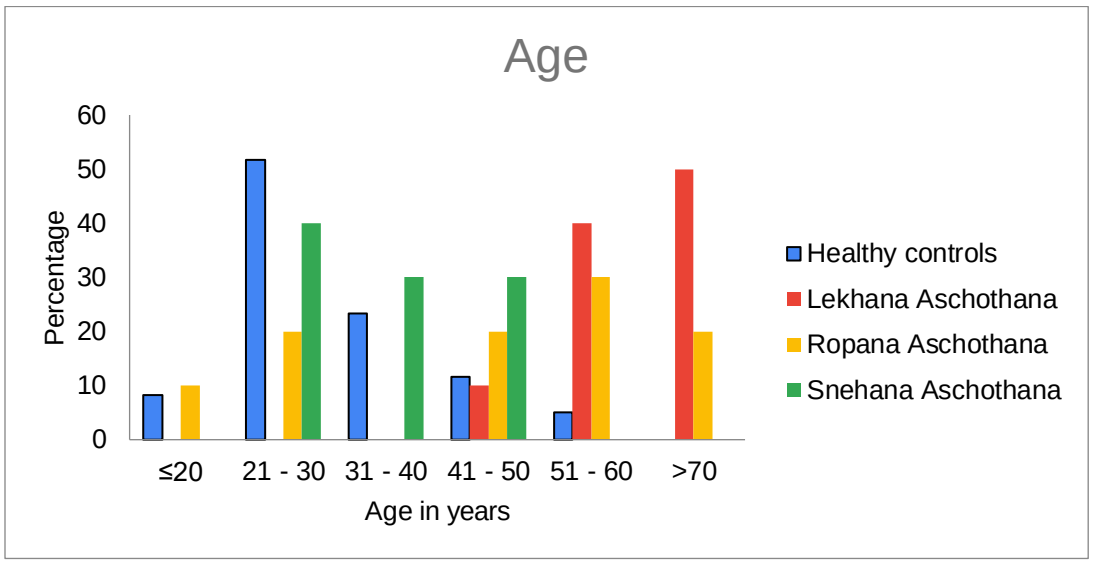
SECTION A: STATISTICAL ANALYSIS OF THE DEMOGRAPHIC DATA

1) AGE

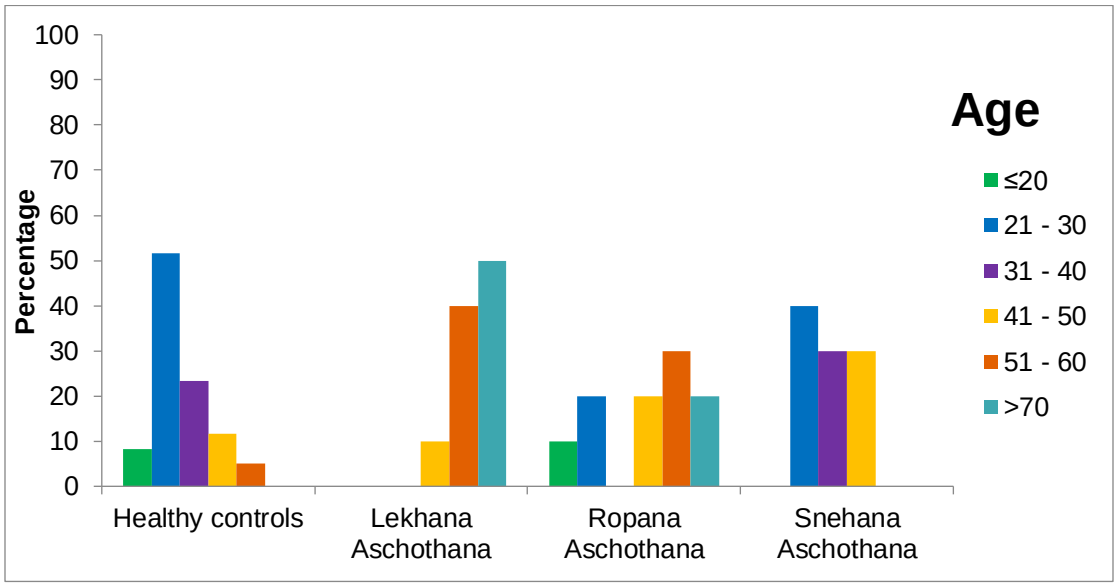
Table- 7.1.1- Distribution of patients based on age

Age in years	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
≤20	5	8.3	0	0	1	10	0	0	6	6.7
21 – 30	31	51.7	0	0	2	20	4	40	37	41.1
31 – 40	14	23.3	0	0	0	0	3	30	17	18.9
41 – 50	7	11.7	1	10	2	20	3	30	13	14.4
51 – 60	3	5	4	40	3	30	0	0	10	11.1
>70	0	0	5	50	2	20	0	0	7	7.8
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.1 & 7.1.2- Distribution of patients based on age



Graph- 7.1.2



As per the test, age is a relevant factor in the study. (p-value is 0.000)

The majority of healthy volunteers are included under the age of 21-30 and very less in the age group of 51-60.

Aschothana had done in diseased individuals requiring snehana , ropana and lekhana aschothana. Among these snehana, aschothana patients came under the age group of 30-50.

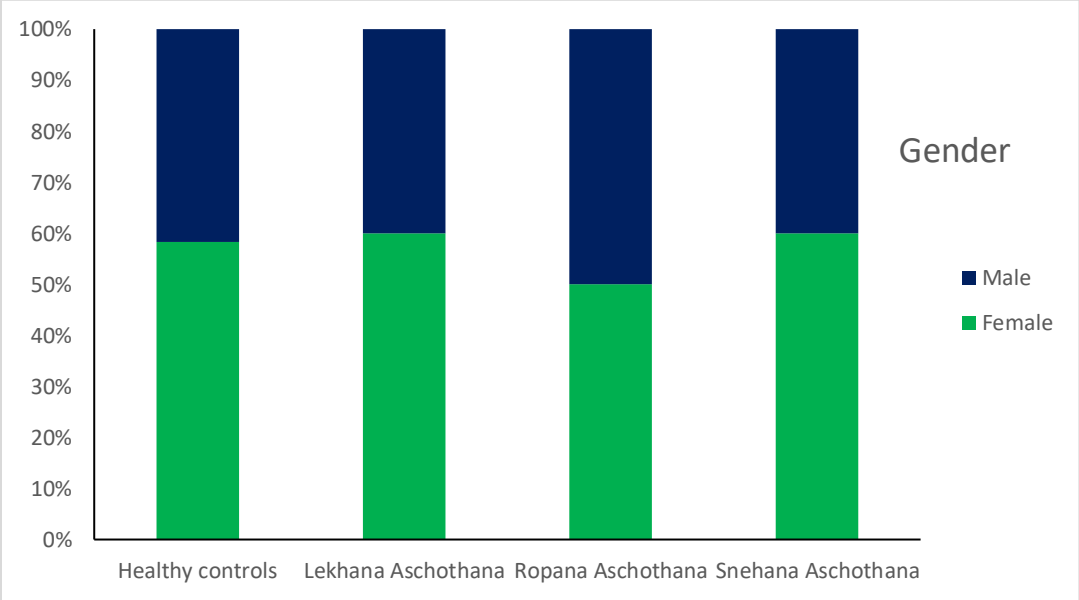
Ropana aschothana indicated patients are distributed without specificity of age. But lekhana aschothana mainly indicated above the age group of 60.

2) SEX

Table-7.1.2 Distribution of patients based on sex

SEX	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
Female	35	58.3	6	60	5	50	6	60	52	57.8
Male	25	41.7	4	40	5	50	4	40	38	42.2
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.3 - Distribution of patients based on sex



As per the results, sex is not a significant variable in the study. (p- value .961)

Healthy individuals, as well as diseased persons of this study, are distributed almost equally in the study.

Healthy individuals -Males- 58.3 %,Females- 41.7 %

Lekhana Aschothana-Males- 60%,Females-40%

Ropana Aschothana- Males- 50 %.Females- 50%

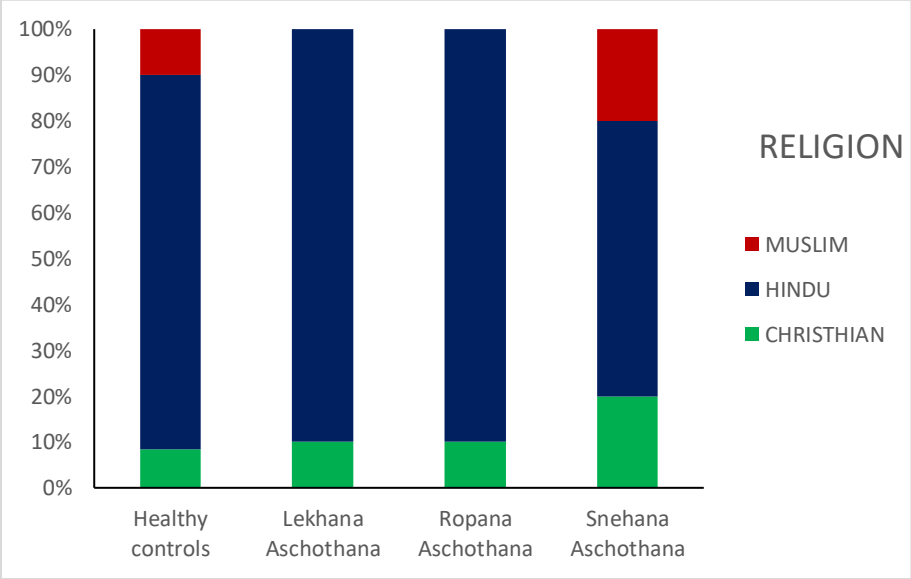
Snehana Aschothana-Males- 60%,Females-40%

3) RELIGION

Table 7.1.3- Distribution of patients based on religion

RELIGION	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
CHRISTIAN	5	8.3	1	10	1	10	2	20	9	10
HINDU	49	81.7	9	90	9	90	6	60	73	81.1
MUSLIM	6	10	0	0	0	0	2	20	8	8.9
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.4 - Distribution of patients based on religion



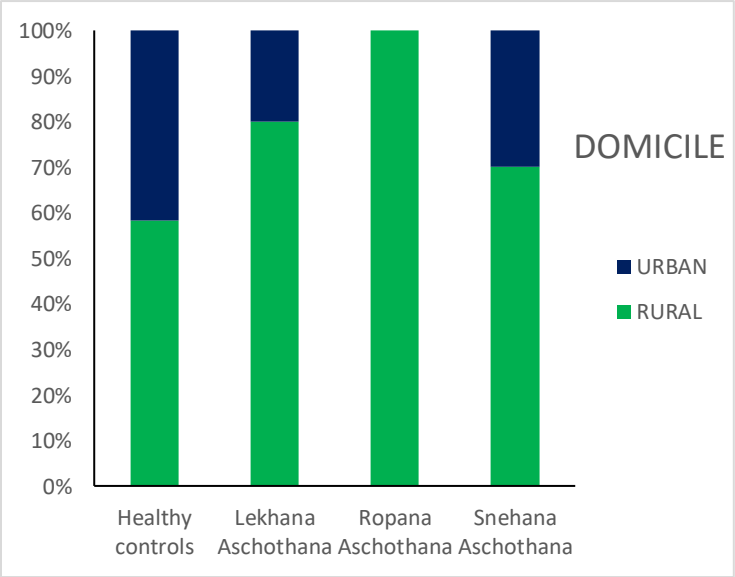
Among 90 patients, 81.7% of healthy individuals are Hindus, 10 % are Muslims and 8.3 % are Christians. In Lekhana Aschothana no Muslim category is obtained, Hindus are 90 % and Christians are 10 %. In Ropana Aschothana also same distribution is obtained. In the case of Lekhana Aschothana, 81.1 % of patients are Hindus, 8.9% of patients are Christians and 10 % are Muslims.

4) DOMICILE

Table 7.1.4- Distribution of patients based on domicile

DOMICILE	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
RURAL	35	58.3	8	80	10	100	7	70	60	66.7
URBAN	25	41.7	2	20	0	0	3	30	30	33.3
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.5 - Distribution of patients based on domicile



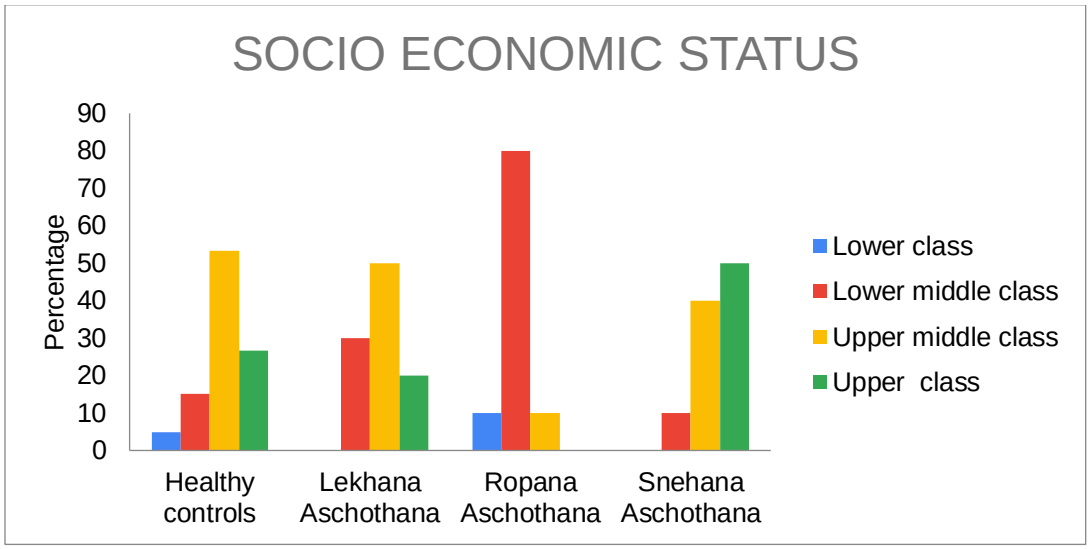
Among healthy individuals 58.3% are urban and 41.7% are rural. In Lekhana Aschothana 80% are urban and 20% are rural. In Ropana Aschothana nobody from the rural population and in Snehana Aschothana 70 % are urban and 30 % are rural.

5) SOCIO-ECONOMICMIC STATUS

Table 7.1.5- Distribution of patients based on socio-economic status

SOCIO ECONOMIC STATUS	Category								Total	
	Healthy controls		Lekhana Aschothan		Ropana Aschothan		Snehana Aschothan			
	N	%	N	%	N	%	N	%	N	%
Lower class	3	5	0	0	1	10	0	0	4	4.4
Lower middle class	9	15	3	30	8	80	1	10	21	23.3
Upper middle class	32	53.3	5	50	1	10	4	40	42	46.7
Upper class	16	26.7	2	20	0	0	5	50	23	25.6
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.6 - Distribution of patients based on socio-economic status



The total number of patients in this study is 90. Among these 4.4% belongs to the Lower class

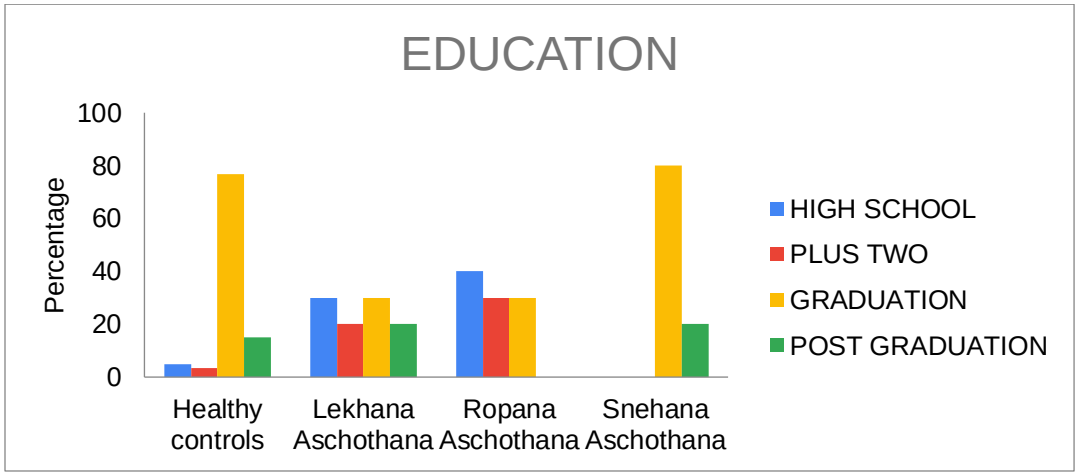
23.3 % belong to Lower Middle Class, 46.7 % are Upper Middle Class and 25.6 % are Upper Class.

6) EDUCATIONAL STATUS

Table 7.1.6-Distribution of Patients based on educational status

EDUCATION	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
HIGH SCHOOL	3	5	3	30	4	40	0	0	10	11.1
PLUS TWO	2	3.3	2	20	3	30	0	0	7	7.8
GRADUATION	46	76.7	3	30	3	30	8	80	60	66.7
POST-GRADUATION	9	15	2	20	0	0	2	20	13	14.4
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.7- Distribution of Patients based on educational status



The educational status of healthy individuals is as follows high school- 5 %, plus two – 3.3%, graduation – 76.7 %, and post-graduation- 15 %. Lekhana Aschothana's high school

category is 30 %, plus two groups are 20 %, graduation and post-graduation are 30 and 20 % respectively. The Ropana Aschothana high school group is 40%, plus two groups are 30 % graduation category is 30 % and post-graduation percentage is zero.

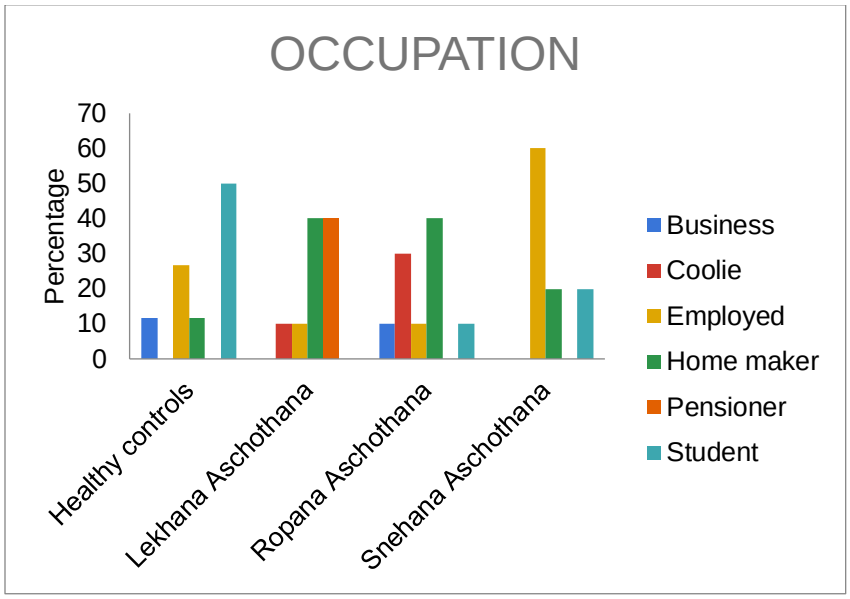
In Snehana Aschothana, the high school group is 10 %, plus the two categories are 7 % and for graduation, post-graduation percentages are 60 and 10 respectively.

7) OCCUPATION

Table-7.1.7 Distribution of patients based on occupation

OCCUPATION	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
Business	7	11.7	0	0	1	10	0	0	8	8.9
Coolie	0	0	1	10	3	30	0	0	4	4.4
Self Employed	16	26.7	1	10	1	10	6	60	24	26.7
Homemaker	7	11.7	4	40	4	40	2	20	17	18.9
Pensioner	0	0	4	40	0	0	0	0	4	4.4
Student	30	50	0	0	1	10	2	20	33	36.7
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.8 - Distribution of patients based on occupation



Different kinds of occupational status were observed among the volunteers – both healthy as well as the diseased one's groups.

It include mainly business/ coolie/ employed/ homemaker/pensioner and students. Healthy individuals are mainly students. The businessmen and homemaker category contribute 11.7 % of the population. Self-employed ones are 26.7 %, and no person belonged to the category of coolie.

In Lekhana Aschothana equal percentage (40%) of patients belonged to the category of pensioner and homemaker. 10 % coolie , and no one from the cateogary of students or businessmen.

In Ropana Aschothana, 10 % for students, businessmen and self employed. Coolie 30 % and homemaker contributed 40 %

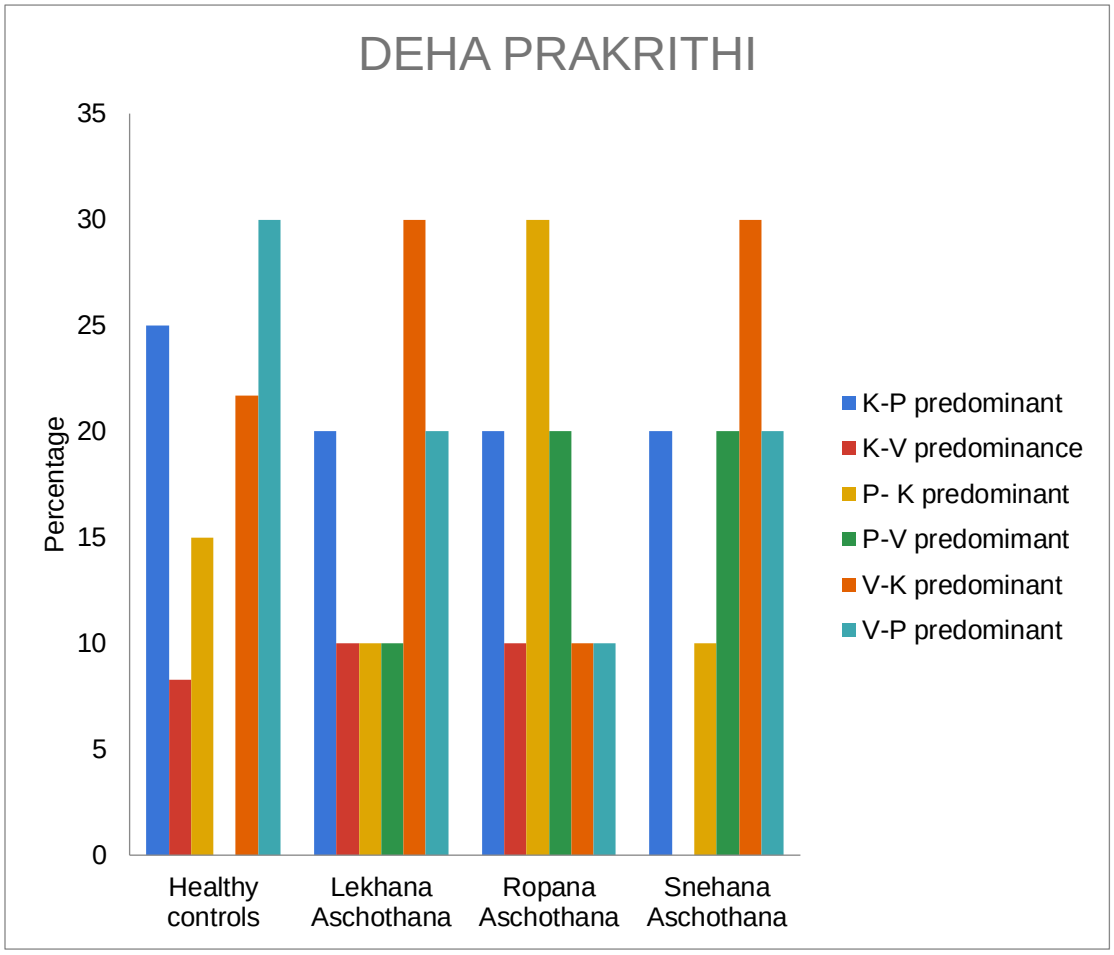
In Snehana Aschothana self-employed, students and homemakers contributed 60,20 and 20 % respectively.

8) DEHA PRAKRITHI

Table 7.1.8- Distribution of patients based on Deha prakrithi

DEHA PRAKRITHI	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
K-P predominant	15	25	2	20	2	20	2	20	21	23.3
K-V predominance	5	8.3	1	10	1	10	0	0	7	7.8
P- K predominant	9	15	1	10	3	30	1	10	14	15.6
P-V predomimant	0	0	1	10	2	20	2	20	5	5.5
V-K predominant	13	21.7	3	30	1	10	3	30	20	22.2
V-P predominant	18	30	2	20	1	10	2	20	23	25.6
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.9- Distribution of patients based on Deha prakrithi



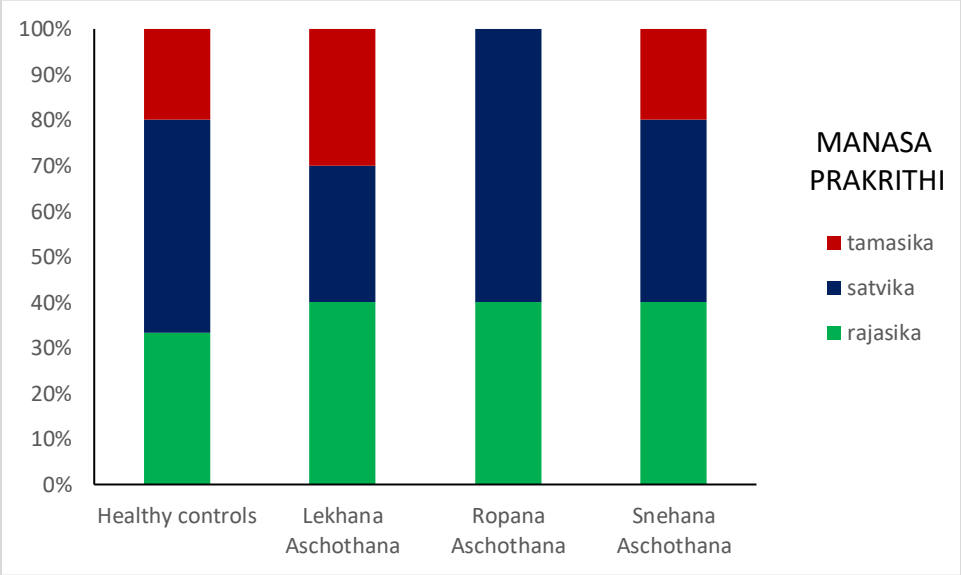
Deha prakrithi analysis revealed different kinds of prakrithi like K-P/ K-V/P-K/P-V/V-K and V-P for the volunteers. Among this vata kapha , pitha- kapha and vata pitha contributions are more.

9) MANASA PRAKRITHI-

Table 7.1.9 -Distribution of patient based on manasa prakrithi

MANASA PRAKRITHI	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
Rajasika	20	33.3	4	40	4	40	4	40	32	35.6
Satvika	28	46.7	3	30	6	60	4	40	41	45.6
Tamasika	12	20	3	30	0	0	2	20	17	18.9
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.10 - Distribution of patient based on manasa prakrithi



Manasa prakrithi of total volunteers included in the study are as follows :

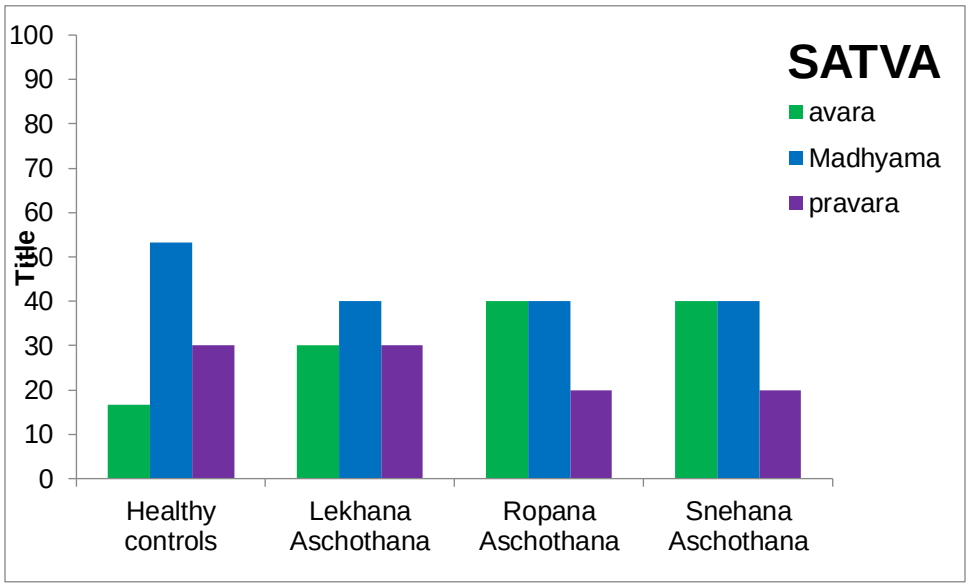
Tamasika- 18.9 %, rajasika- 35.6 % and satvika 45.6 %

10) SATVA

Table 7.1.10- Distribution of patients based on satva

SATVA	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
Avara	10	16.7	3	30	4	40	4	40	21	23.3
Madhyama	32	53.3	4	40	4	40	4	40	44	48.9
Pravara	18	30	3	30	2	20	2	20	25	27.8
Total	60	100	10	100	10	100	10	100	90	100

Graph**7.**1.11 - - Distribution of patients based on satva



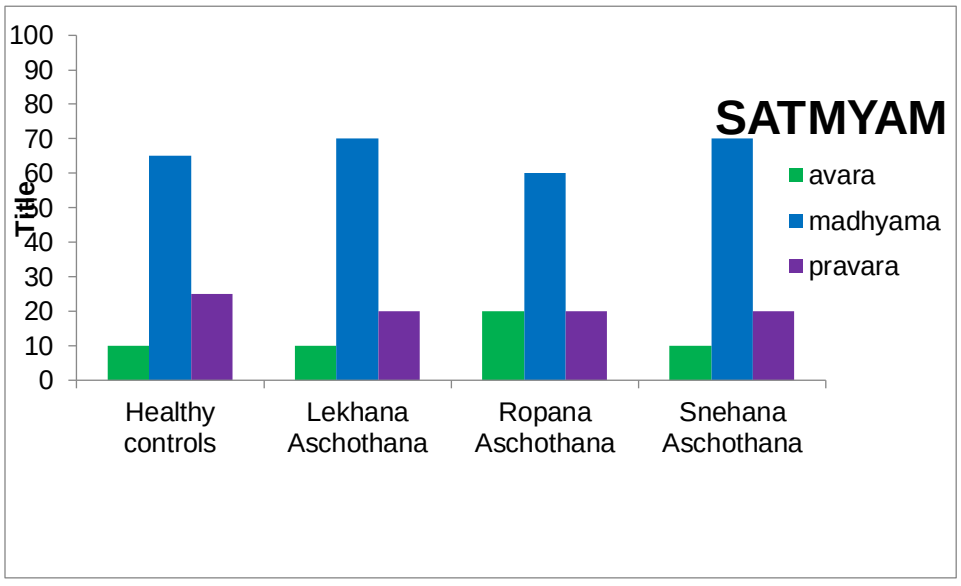
Based on satva there are three cateogaries – pravara, madhyama, and avara. Total volunteers who belong to the group of pravara satva is 27.8 % and madhyama satva is 48.9 % and avara satva is 23.3 %

11) SATMYA

Table 7.1.11- Distribution of patients based on satmya

SATMYAM	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
Avara	6	10	1	10	2	20	1	10	10	11.1
Madhyama	39	65	7	70	6	60	7	70	59	65.6
Pravara	15	25	2	20	2	20	2	20	21	23.3
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.12 - - Distribution of patients based on satmya



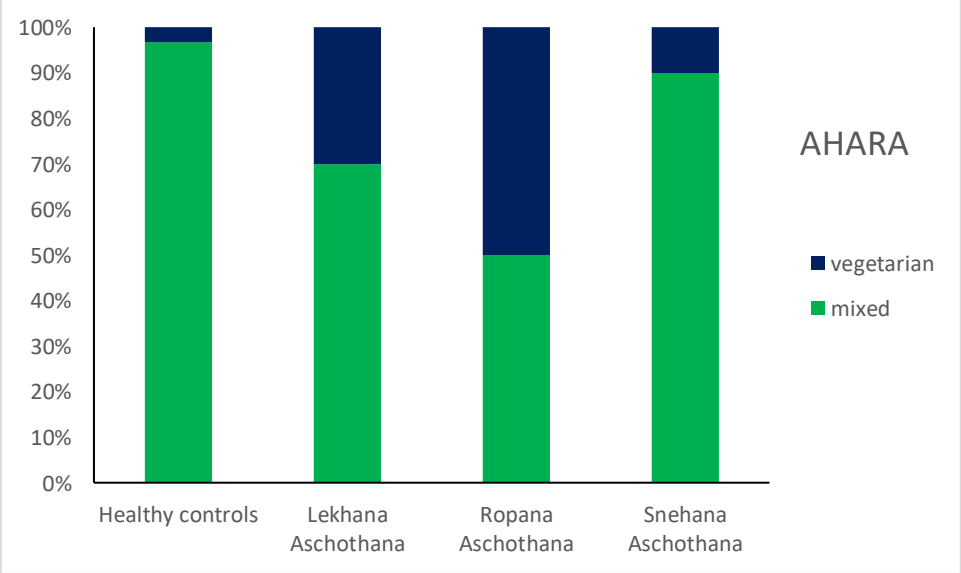
Among satmya, three groups are obtained. Similar to satva it is pravara madhyama and avara. The percentage of total volunteers belonged under pravara satmya 23.3 % , madhyama satmya is 65.6 % and avara satmya is 11.1 %.

12) AHARA

Table 7.1.12- Distribution of patients based on ahara

AHARA	Category								Total	
	Healthy controls		Lekhana Aschothana		Ropana Aschothana		Snehana Aschothana			
	N	%	N	%	N	%	N	%	N	%
mixed	58	96.7	7	70	5	50	9	90	79	87.8
vegetarian	2	3.3	3	30	5	50	1	10	11	12.2
Total	60	100	10	100	10	100	10	100	90	100

Graph 7.1.13 - - Distribution of patients based on ahara



On the basis of ahara, two cateogaries are obtained. Mixed and vegetarian. In the group of mixed, 96. 7 % of healthy volunteers are included. And rest goes to vegetarian cateogary- 3.3 %

In the group of Lekhana Aschothana, the percentage of mixed and vegetarian people is 70 and 30 % respectively.

In the group of Ropana Aschothana percentage of both of these cateogaries are equal and is 50 %

In the last group of Snehana Aschothana, percentage of mixed group is 90 % and vegetarian cateogary is 10 %

SECTION B –ANALYSIS BASED ON PROCEDURE OF ASCHOTHANA

In this section analysis of results obtained as a part of

- **standardization of pichu varthi**
- **comparison of dropper bottle with Pichu varthi method**
- **Analysis of exophthalmometric values**
- **Analysis of Prakrithic features of eye**
- **Analysis of Liquid Holding Capacity of Healthy Volunteers**
- **Analysis of Aschothana at Drik Madhya and Kaneenaka**

- STANDARDIZATION OF PICHU VARTHI

For doing standardization of Pichu Varthi, two factors are considered. One is the material used for making pichu varthi and the other is size of pichu varthi.

Material used for making pichu varti

For these different materials are used, like cotton/ gauze/ cotton cloth and kora cloth. Among this gauze is found to be ideal due to the following reasons

1. While analyzing the rate of flow of liquid from pichu varthi made up of cotton , an uncontrolled flow is obtained.
2. Cotton cloth and kora cloth take more time to get wet and in media like honey very scanty flow is obtained.
3. Gauze helped in a controlled flow of medicine in all media

Size of pichu varthi

The length of Pichu varthi is fixed as 10 cm as length of the long beak like portion through it medicines are poured is 7 cm and the height of procedure is 2 A or 2&1.76 cm and we can take 10 cm as the wick length

Taking too much breadth more than that of the length of sukthi, can interfere a free flow of medicine.

Aschothana can be done using different media, so the viscosity of all media may not be the same. Therefore interference of flow of medicine freely through the varthi can further interfere the procedure of aschothana.

Different breadths are tried. While analysing the number of drops obtained in 2 minutes of time, ideal size can be taken as 10* 5 cm. Increase in breadth can result in scanty flow especially in high viscous media like honey, and very less breadth can cause uncontrolled flow.

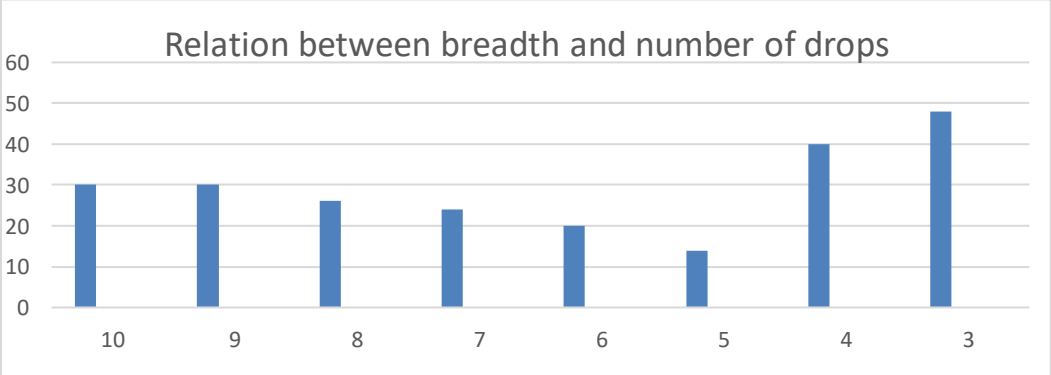
Obtained datas are tabulated

Table 7.2.1 Length and breadth of different types of varthis with number of drops obtained for 2 minutes of time

LENGTH (cm)	BREADTH (cm)	NUMBER OF DROPS OBTAINED IN 2 MINUTES OF TIME
10	10	30
10	9	30
10	8	26
10	7	24
10	6	20
10	5	14
10	4	40
10	3	48

Graph ploted using different breadths taken for pichu varthi and number of drops

Graph 7.2.1 - relation between breadth and number of drops



- COMPARISON OF DROPPER BOTTLE WITH PICHU VARTHI

Using different media, pichu varthi method is compared with dropper bottle method. 30 drops are allowed to fall over an empty bowl and the resultant quzntity is measured using a micropipette.

The so obtained result is as follows

Table 7.2.2 – comparison of pichu varthi with eyedropper bottle method

MEDIA	NO.OF DROPS	DROPPER BOTTLE METHOD(qty in ml)	PICHU VARTHI METHOD (qty in ml)
STERILE WATER	30	2	1.75
HONEY	30	1	0.75
GHEE	30	1.5	1.3
MRIDWEEKADI KASHAYA	30	2	1.80
TRIPHALA ARKA	30	2.3	2

According to the result, quantity of different kinds of medicine obtained is nearly the same for pichu varthi and dropper bottle method. So we can adopt dropper bottle method by considering safety aspects of the procedure.

❖ ANALYSIS OF PRAKRITHIC FEATURES OF EYE

Analysis of features of the eye for all volunteers is taken qualitatively, using a tool adopted from research articles. Dripping medicine at Kaneenaka Sandhi is depended on the size and shape of the eyes based on prakrithi. The main characteristic feature of Vata dosha predominant eye is small size , medium-sized for pitha ,and wide in kapha. But ekadoshaja prakrithi is very difficult to obtain and all persons have mixed features. Prakrithi is a qualitative variable, unlike exophthalmometry. Therefore accurate measurement is difficult and varies based on the tool as well as assessment by the observer.

The quantitative scoring of prakrithic features couldn't do as the study mainly focused on exophthalmometry as the major factor in determining the size of the eye.

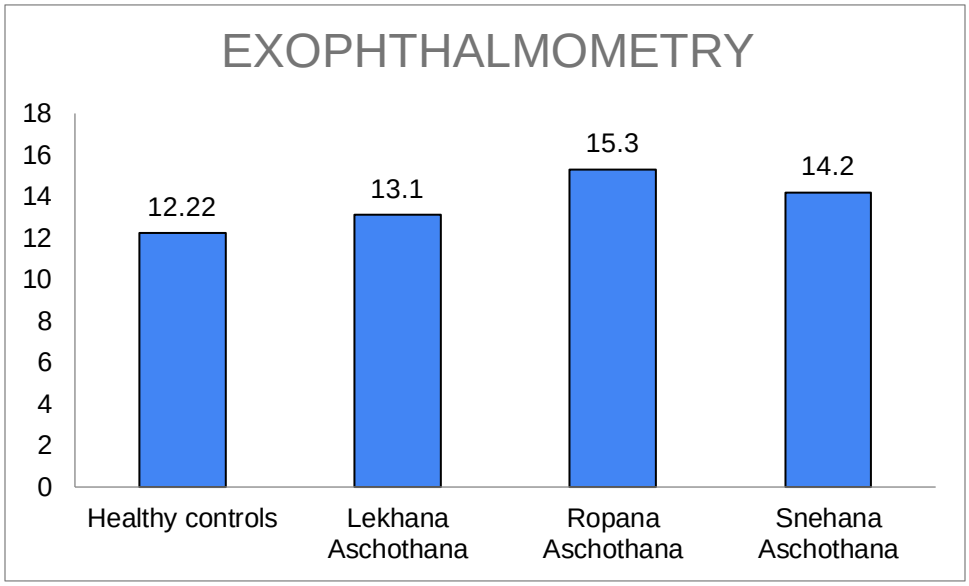
❖ ANALYSIS OF EXOPHTHALMOMETRIC VALUES

Table 7.2.3- analysis of exophthalmometric values of total volunteers

Category	N	EXOPHTHALMOMETRY		P
		Mean	Sd	
Healthy controls	60	12.22	1.18	<0.001
Lekhana Aschothana	10	13.1	1.37	
Ropana Aschothana	10	15.3	4.057	
Snehana Aschothana	10	14.2	1.619	

+

Graph 7.2.2 – analysis of exophthalmometric values



Exophthalmometric measurements were taken for all volunteers using Leudde Exophthalmometer. The normal range lies between 12-21 mm. in healthy volunteers average value of exophthalmometry is 12.22mm. 60 patients with no ocular or systemic complaints were selected as healthy volunteers.

In Lekhana Aschothana average value of 10 volunteers have the value of 13.1 mm.

In Ropana Aschothana average value is 15.3 and in Snehana Aschothana it is 14.2 mm

On multiple comparison healthy voulnteers are compared with diseased category like lekhana aschothana , ropana aschothana and snehana aschothana indicated patients. The obtained mean differences and standard error are enlisted as follows :

Table 7.2.4 – Multiple comparison of exophthalmometric values among volunteers

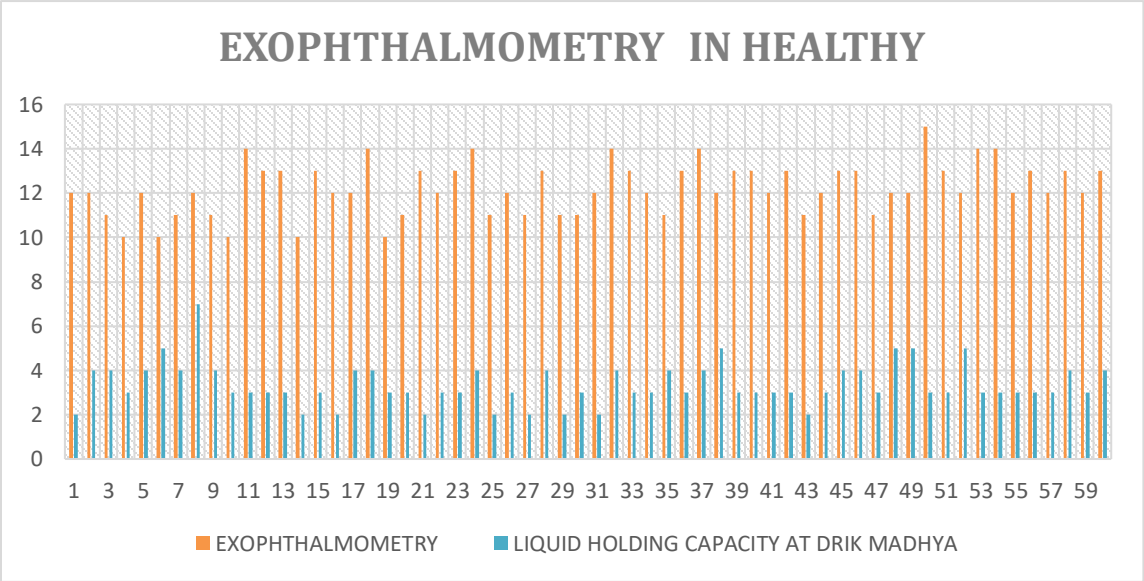
Multiple comparison	Mean Difference	Se	P
Healthy controls VS Lekhana Aschothana	0.883	0.606	0.149
Healthy controls VS Ropana Aschothana	3.083	0.606	<0.001
Healthy controls VS Snehana Aschothana	1.983	0.606	0.002
Lekhana Aschothana VS Ropana Aschothana	2.2	0.794	0.007
Lekhana Aschothana VS Snehana Aschothana	1.1	0.794	0.169
Ropana Aschothana VS Snehana Aschothana	1.1	0.794	0.169

As already mentioned exophthalmometric values are important when aschothana is performed at Drik Madhya.

In healthy volunteers exophthalmometric values have got a mean of 12.2 mm

A Graph is plotted with Exophthalmometric values with Liquid holding capacity of eye at Drik Madhya

Graph 7.2.3 – exophthalmometric values with liquid holding capacity of eye at drik Madhya in healthy volunteers



In Healthy volunteers, the value lies in the range of 12-14 mm, and the liquid holding capacity of eyes at Drik Madhya is a maximum of 4 drops. 98% of persons obtained even in the group of the diseased category(30-90 patients) are also having normal range of values. The mean values of 13.1 and 14.3 in the Lekhana and Snehana Aschothana groups emphasize that point.

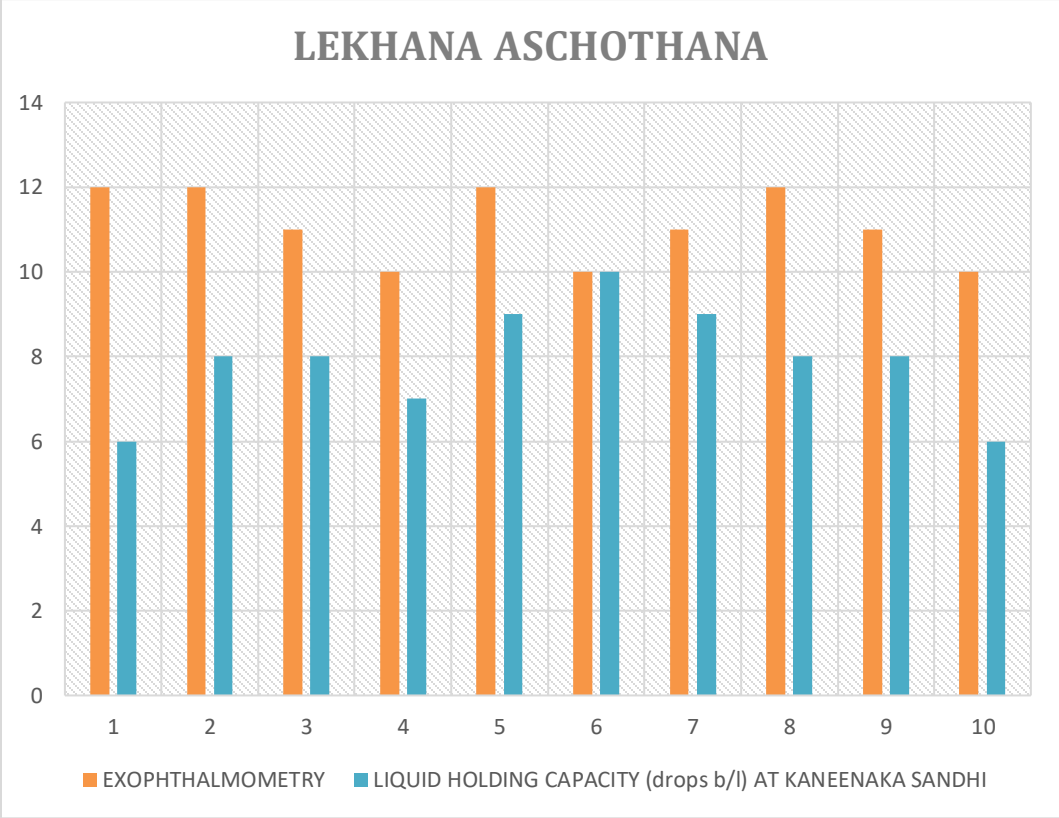
In the group of Ropana Aschothana, one selected patient has values in the range of 29 mm which is different from the normal values. Therefore mean and mean differences have got little high value on comparing with the other two.

- EXOPHTHALMOMETRY AND LIQUID HOLDING CAPACITY AT DRIK MADHYA IN LEKHANA ASCHOTHANA

Table 7.2.5 - Exophthalmometry and liquid holding capacity at Drik Madhya in Lekhana Aschothana

EXOPHTHALMOMETRY	NO.OF DROPS OBTAINED
13	4
16	2
11	2
12	3
13	2
14	3
13	2
12	2
13	2
14	3

Graph 7.2.4 – exophthalmometry and liquid holding capacity at drik Madhya in Lekhana aschothana



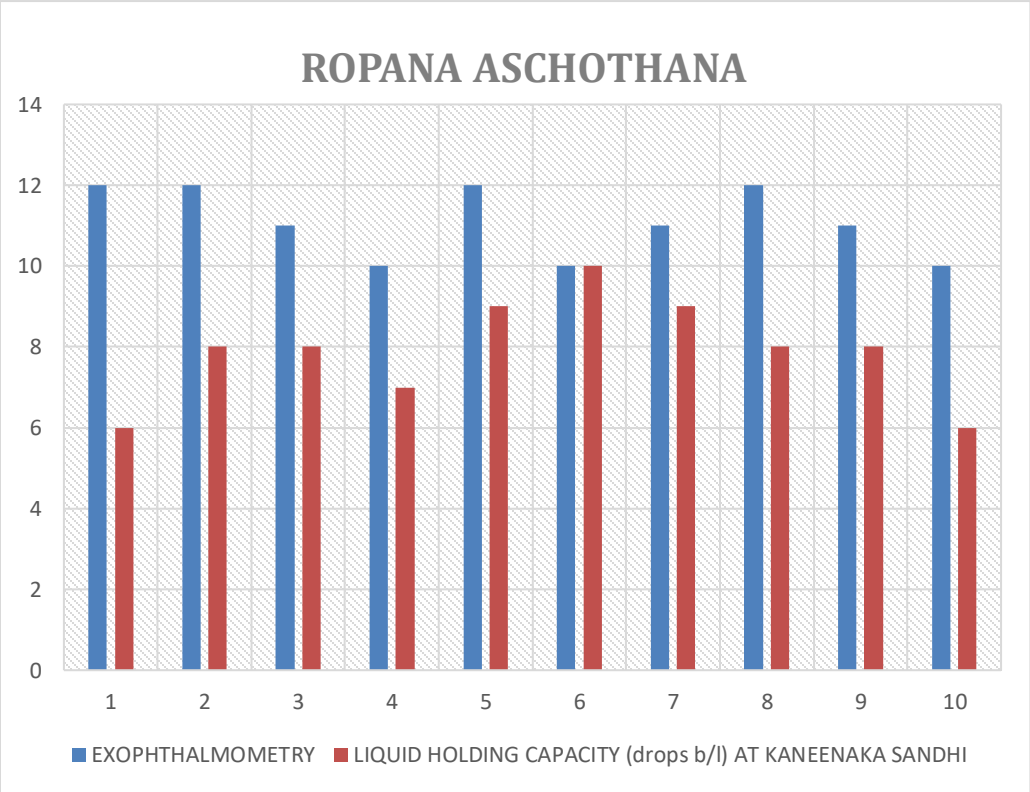
On analysing the graph it is found that on increased exophthalmometric values, less number is possible.

- EXOPHTHALMOMETRY AND LIQUID HOLDING CAPACITY AT DRIK MADHYA IN ROPANA ASCHOTHANA

Table 7.2.6 - Exophthalmometry and liquid holding capacity at Drik Madhya in Ropana Aschothana

EXOPHTHALMOMETRY	NO.OF DROPS OBTAINED
12	4
29	2
16	4
14	3
11	3
13	3
13	3
16	2
15	3
14	3

Graph 7.2.5 - exophthalmometry and liquid holding capacity at drik Madhya in Ropana aschothana



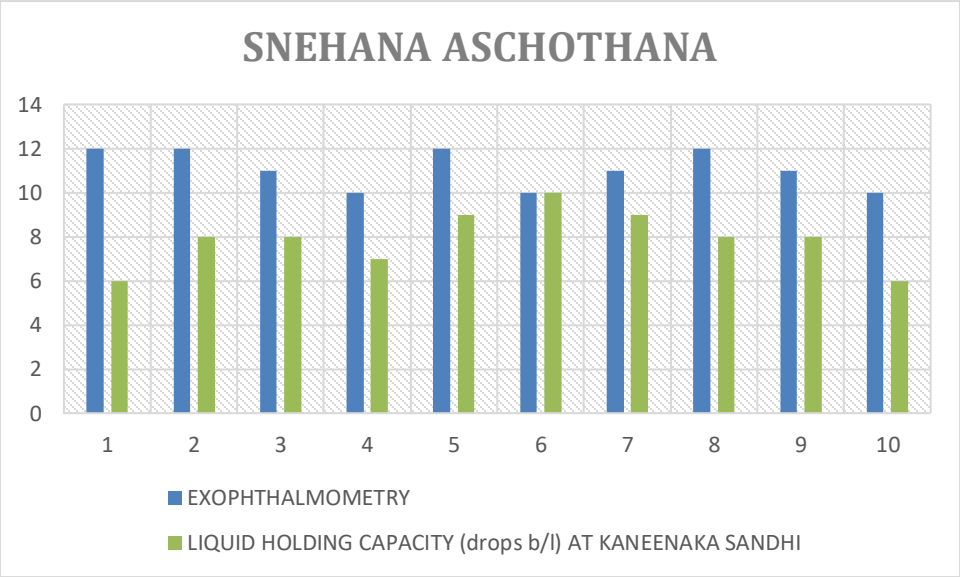
Here also if more the exophthalmometry less is the dose possible to be held..

- EXOPHTHALMOMETRY AND LIQUID HOLDING CAPACITY AT DRIK MADHYA IN SNEHANA ASCHOTHANA

  Table 7.2.7 - Exophthalmometry and liquid holding capacity at Drik Madhya in Snehana Aschothana

EXOPHTHALMOMETRY	NO.OF DROPS OBTAINED
12	4
29	2
16	4
14	3
11	3
13	3
13	3
16	2
15	3

Graph 7.2.6 - exophthalmometry and liquid holding capacity at drik Madhya in Snehana aschothana



In the category of Snehana aschothana one value obtained less than normal range ie; 10 mm for that around 5 drops could be possible.

On analysing the graphs, relation between exophthalmometry and number of drops applied at drik Madhya have a negative relation as exophthalmometry increases, only less number is possible.

- ❖ LIQUID HOLDING CAPACITY AT KANEENAKA SANDHI WITH EXOPHTHALMOMETRIC VALUES – HEALTHY VOLUNTEERS

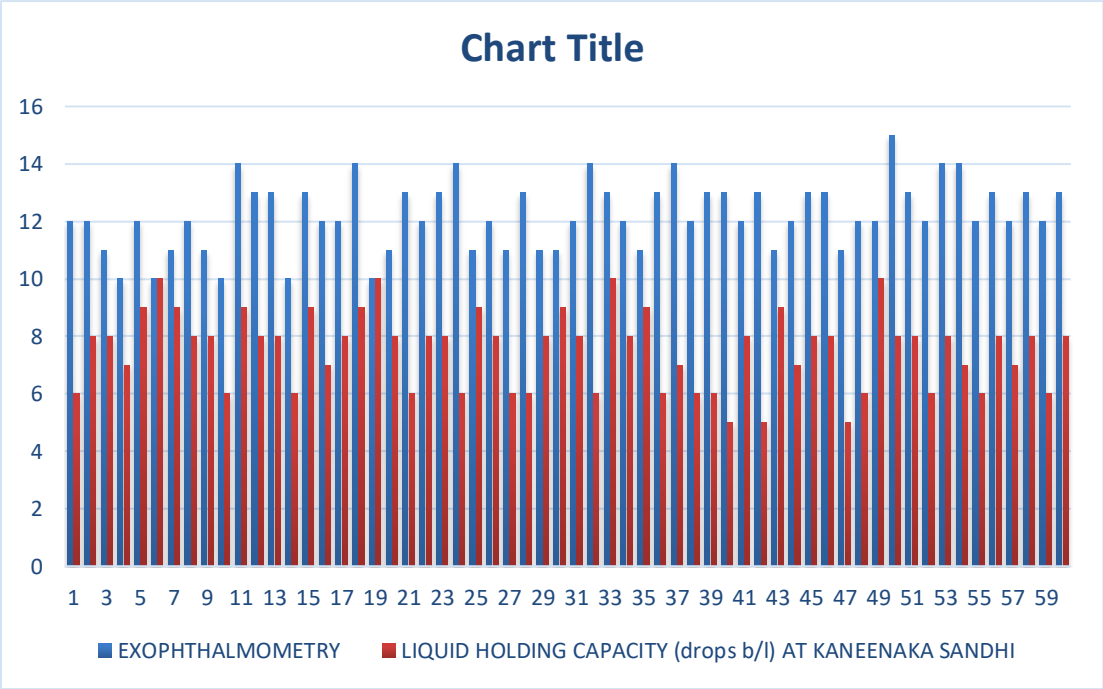
Table 7.2.8 - liquid holding capacity at kaneenaka sandhi with exophthalmometric values – healthy volunteers

EXOPHTHALMOMETRY (mm b/l)	LIQUID HOLDING CAPACITY (drops b/l) AT KANEENAKA SANDHI
12	6
12	8
11	8
10	7
12	9
10	10
11	9

12	8
11	8
10	6
14	9
13	8
13	8
10	6
13	9
12	7
12	8
14	9
10	10
11	8
13	6
12	8
13	8
14	6
11	9
12	8
11	6
13	6
11	8
11	9
12	8
14	6
13	10
12	8
11	9
13	6
14	7
12	6
13	6

13	5
12	8
13	5
11	9
12	7
13	8
13	8
11	5
12	6
12	10
15	8
13	8
12	6
14	8
14	7
12	6
13	8
12	7
13	8
12	6
13	8

Graph 7.2.7 - exophthalmometry and liquid holding capacity at Kaneenaka sandhi in healthy volunteers

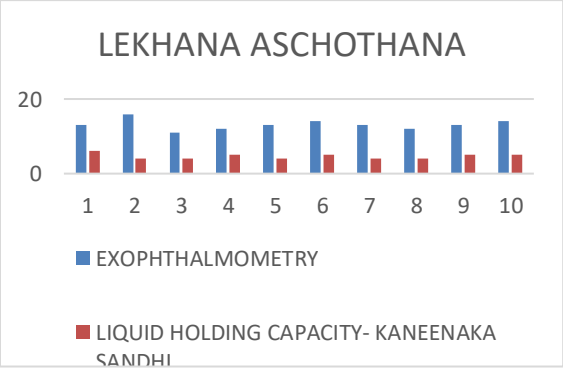


- LIQUID HOLDING CAPACITY AT KANEENAKA SANDHI WITH EXOPHTHALMOMETRIC VALUES – LEKHANA ASCHOTHANA

Table 7.2.9 – exophthalmometry with liquid holding capacity at Kaneenaka in Lekhana aschothana

EXOPHTHALMOMETRY	LIQUID HOLDING CAPACITY- KANEENAKA SANDHI
13	6
16	4
11	4
12	5
13	4
14	5
13	4
12	4
13	5
14	5

Graph 7.2.8- exophthalmometry with liquid holding capacity at Kaneenaka in Lekhana aschothana

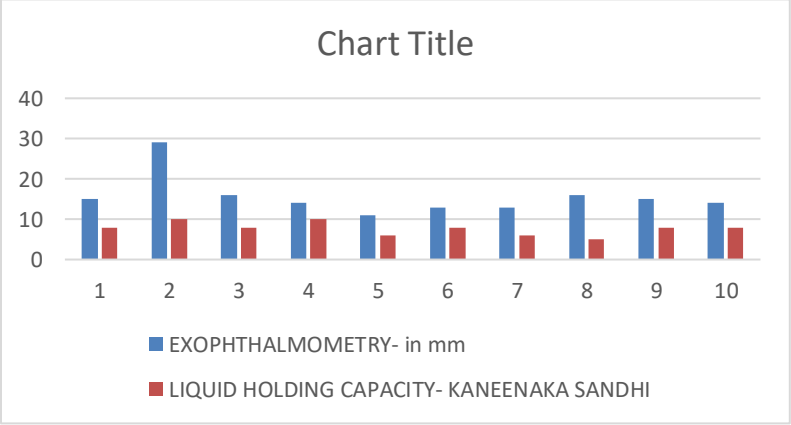


- LIQUID HOLDING CAPACITY AT KANEENAKA SANDHI WITH EXOPHTHALMOMETRIC VALUES – ROPANA ASCHOTHANA

Table 7.2.10 - liquid holding capacity at kaneenaka sandhi with exophthalmometric values – ropana aschothana

EXOPHTHALMOMETRY- in mm	LIQUID HOLDING CAPACITY- KANEENAKA SANDHI
15	8
29	10
16	8
14	10
11	6
13	8
13	6
16	5
15	8
14	8

Graph 7.2.9- liquid holding capacity at kaneenaka sandhi with exophthalmometric values – ropana aschothana

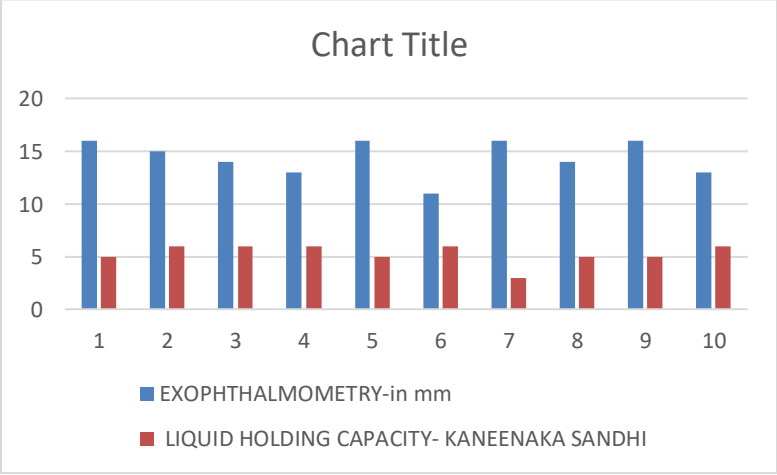


- ❖ LIQUID HOLDING CAPACITY AT KANEENAKA SANDHI WITH EXOPHTHALMOMETRIC VALUES- SNEHANA ASCHOTHANA

Table 7.2.11 - liquid holding capacity at kaneenaka sandhi with exophthalmometric values- snehana aschothana

EXOPHTHALMOMETRY- in mm	LIQUID HOLDING CAPACITY- KANEENAKA SANDHI
16	5
15	6
14	6
13	6
16	5
11	6
16	3
14	5
16	5
13	6

Graph 7.2.10 -liquid holding capacity at kaneenaka sandhi with exophthalmometric values- snehana aschothana



On analysing the graphs relation between exophthalmometry and number of drops applied at Kaneenaka sandhi have not much significant relation

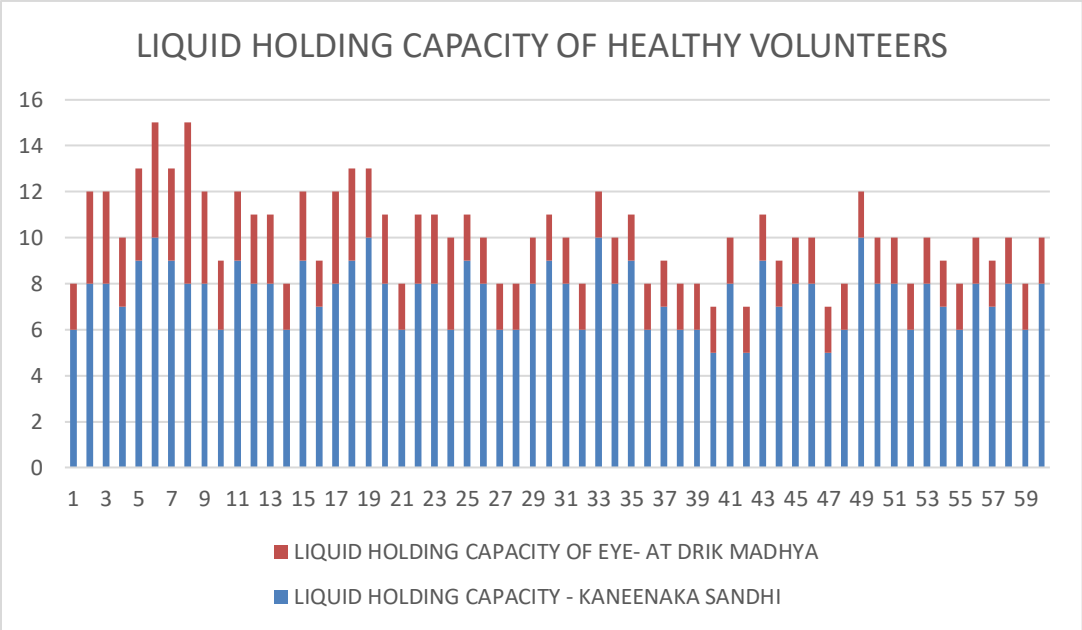
- COMPARISON OF LIQUID HOLDING CAPACITY OF HEALTHY VOLUNTEERS AT TWO SITES

The liquid holding capacity of eye for healthy individuals at kaneenaka sandhi or inner canthus of eye , and drik Madhya or pupillary area is analysed with exophthalmometric measurements.

Table 7.2.12-Liquid holding capacity of 60 healthy volunteers at kaneenaka sandhi and Drik Madhya

SITE OF DOING ASCHOTHANA	MEAN	STANDARD DEVIATION
Kaneenaka Sandhi	7.53	1.334
Drik Madhya	3.35	0.954

Graph 7.2.11 – comparison of liquid holding capacity of healthy volunteers at two sites



The average number of drops obtained at Kaneenaka Sandhi for 60 healthy volunteers is 7.53 with a standard deviation of 1.334

The average number of drops obtained at Drik Madhya or Pupillary area of the eye in healthy volunteers is 3.35 with a standard deviation of 0.954

- ❖ COMPARISON OF LIQUID HOLDING CAPACITY IN LEKHANA ASCHOTHANA

Lekhana Aschothana had tried in patients having

Cataract/ concretions & follicles of eye lid / and in conditions like subconjunctival hemorrhages. Mainly lekhana aschothaa provided at OP of Shalakya Department Of Government Ayurveda College Thripunithura are – triphala arka/ sarkara mastu kshoudra combinations and so on.

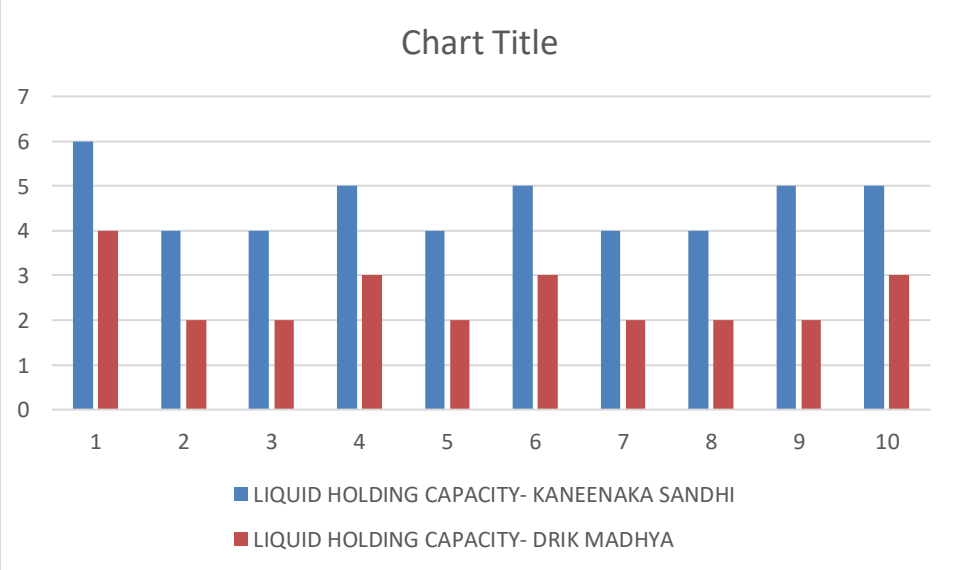
10 patients are selected from op and are subjected to case taking, exophthalmometric measurements and aschothana kalpa.

The results obtained are

Table 7.2.13- Liquid holding capacity of 10 volunteers at Kaneenaka sandhi and at Drik Madhya in Lekhana Aschothana

SITE OF DOING Aschothana	MEAN	STANDARD DEVIATION
Kaneenaka Sandhi	4.6	0.699
Drik Madhya	2.5	0.707

Graph 7.2.12 comparison of liquid holding capacity of Lekhana Aschothana at two sites



- ❖ COMPARISON OF LIQUID HOLDING CAPACITY IN ROPANA ASCHOTHANA

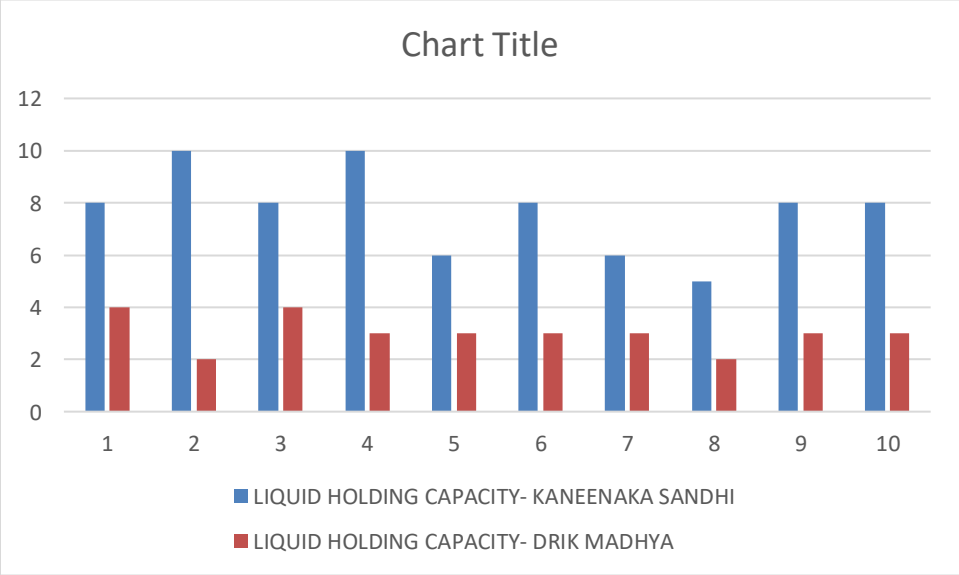
Ropana aschothana indicated 10 patients were selected from OPD and are subjected to do aschothana with commonly used aschothana yogas like Mridweekadi arka, Chandanadi aschothana.

The two methods were tried and result is obtained as

Table 7.2.14- liquid holding capacity of 10 volunteers at Drik Madhya and at Kaneenaka Sandhi in Ropana Aschothana

SITE OF ASCHOTHANA	MEAN	STANDARD DEVIATION
Kaneenaka Sandhi	7.7	1.636
Drik Madhya	3	0.667

Graph 7.2. 13 - comparison of liquid holding capacity of Ropana aschothana at two sites



- ❖ COMPARISON OF LIQUID HOLDING CAPACITY IN SNEHANA ASCHOTHANA

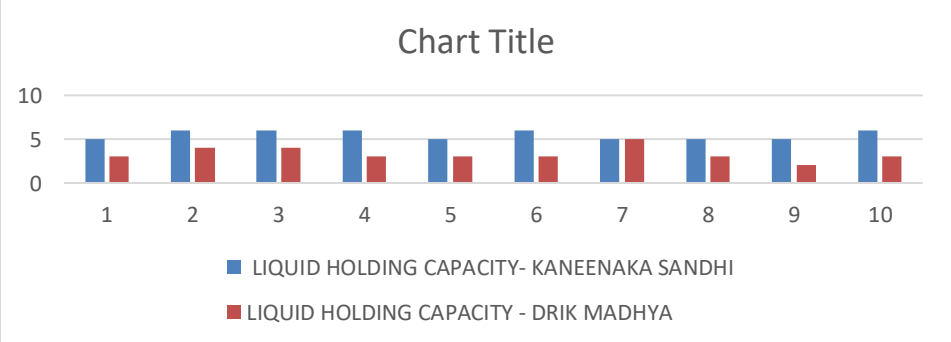
Snehana aschothana is commonly indicated for vata dosha predominant conditions as per classics. Mainly durva ghritha, thraiphala ghritha, maha thraiphala ghritha, jeevanthyadi ghritha, patoladi ghrtiha are prescribed for patients depending upon the status of each dosha.

10 patients are selected and snehana aschothana had done. Results are tabulated as :

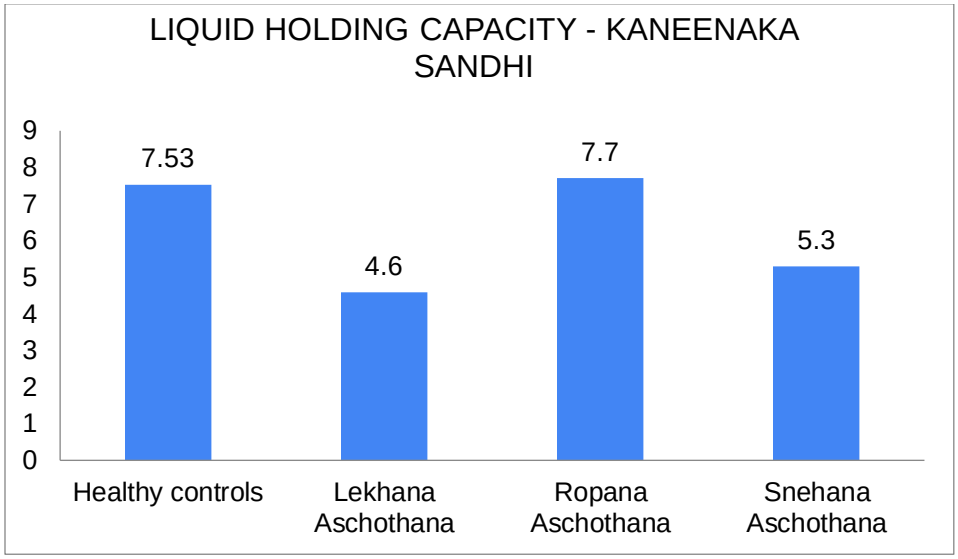
Table 7.2.15 - liquid holding capacity of 10 volunteers at Drik Madhya and at Kaneenaka Sandhi in Snehana Aschothana

SITE OF DOING ASCHOTHANA	MEAN	STANDARD DEVIATION
Kaneenenaka Sandhi	5.3	0.949
Drik Madhya	3.4	1.075

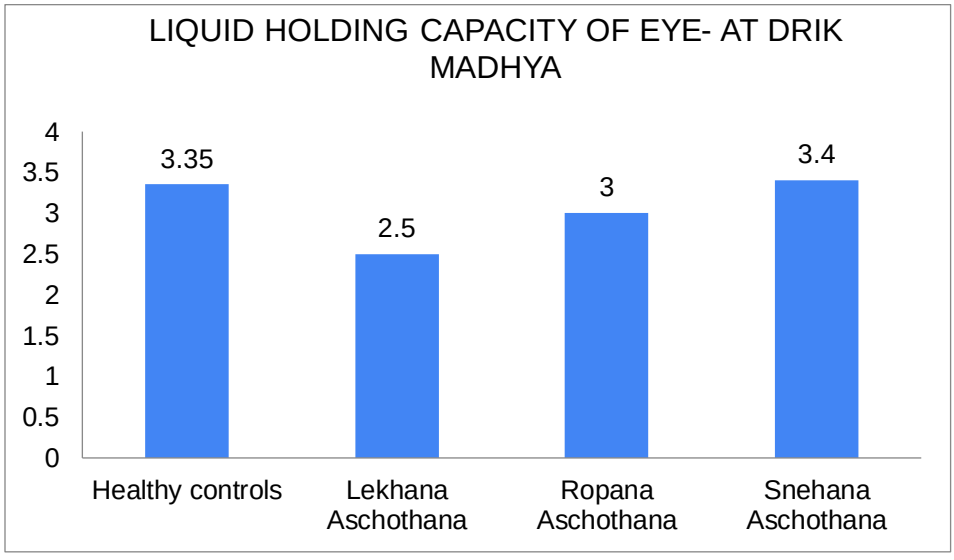
Graph 7.2.14 - comparison of liquid holding capacity of Snehana Aschothana at two sites



Graph 7.2.15 – average value of liquid holding capacity of all volunteers – Kaneenaka sandhi



Graph 7.2.16 - – average value of liquid holding capacity of all volunteers – drik madhya



the relation between exophthalmometric values and site of application of Aschothana among volunteers are tested using spearman correlation coefficient.

Table- 7.2.16 - Exophthalmometry with liquid holding capacity at drik Madhya spearman correlation coefficient

Exophthalmometry with liquid holding capacity at drik Madhya	Spearman correlation coefficient (r)
Healthy volunteers	-0.118
Lekahana Aschothana	-0.04
Ropana Aschothana	-0.05
Snehana Aschothana	-0.33

As per the correlation coefficient, negative relation is existing between exophthalmometry and liquid holding capacity at drik Madhya.

Table7.2.17 - Exophthalmometry with liquid holding capacity at kaneenka sandhi- spearman correlation coefficent

Exophthalmometry with liquid holding capacity at Kaneenaka sandhi	Spearman correlation coefficient (r)
Healthy volunteers	0.12
Lekahana Aschothana	0.03
Ropana Aschothana	0.05
Snehana Aschothana	0.0456

On the basis of the test, statistical relationship between exophthalmos and number of drops possible at Kaneenaka sandhi is insignificant.

Finally by concluding the two sites of Aschothana as per the classics include drik Madhya and Kaneenaka sandhi. Dose range close to classical mentioned quantity is possible at Kaneenaka sandhi. At drik Madhya exophthalmos of the eye play a crucial role as the range of exophthalmos increases less number is possible.

DISCUSSION

DISCUSSION

In any research work, it is very important to correlate the findings with the result. So this section comprises critical reasoning of essential points from the conceptual study as well as the result obtained after doing the procedure of Aschothana, in order to draw the specific conclusions of the present work.

DISCUSSION ON SELECTION OF THE PROBLEM

- Shalakya Tantra is one of the most unique branches of Ayurveda dealing with disorders of all supraclavicular regions. Apart from all these regions eyes are said to be the most important and protection of eyesight should be the prime objective
- Managing ocular conditions encompasses topical and systemic therapeutic forms
- Kriyakalpas are a distinct group of topical applications in Ayurveda for the management of diseases related to the eye.
- Among 7 Kriyakalpas Aschothana belongs to the most patient-friendly and economical procedure where medicated drops are instilled into the eyes at the inner canthus (According to Ashtanga Hridaya, Ashtanga Sangraha, and Susrutha)/center of the eye (Sarngadhara Samhitha) that is kept open, from a height of 2A
- There are three kinds of Aschothana – lekhana/ snehana and ropana having doses of 8\10 and 12 bindus. This classification is based on Kapha/ Vata and Pitta dosha predominance respectively.
- As per modern research articles the maximal conjunctival capacity is 30 µl. and the size of one drop is 0.05 ml. So even a single drop of medicine cannot be accommodated into the eyes and the bioavailability of topical application is very less when compared to other modes of ocular drug delivery systems.

- So inclusion of classically mentioned doses is practically found to be difficult on the basis of these findings
- Therefore practical method of Aschothana has deviated from the traditional way to the eyedrop method where maximum drops of 3 are advised for all patients in almost all the diseased conditions
- There are shreds of evidence regarding the traditional practice of Aschothana from ancient times onwards available in classic ayurvedic literature, describing Aschothana in high doses. But specificity regarding the procedure is not available rather two terms are mentioned as *akshi sechana* and *akshi poorana*

- Pilot study conducted prior to this research also revealed the role of Aschothana in acute conditions of the eye in the traditional medicinal system practiced in very high doses as mentioned in classical textbooks.
- As an effective, simple, economic, and patient friendly procedure, the practice of Aschothana in the correct way should be encouraged by checking the methodology of Aschothana in order to dispel the doubts regarding the application of classically mentioned doses for obtaining a standardized result.

DISCUSSION ON PROCEDURE

SECTION A DISCUSSION ON DEMOGRAPHIC DATA

Age

The study includes 90 volunteers. Out of which 60 are healthy volunteers. A major portion of the healthy volunteers are included under the age of 21-30 and very less in the age group

of 51-60. Natural aging changes affect eye after 40 years. Therefore getting healthy volunteers after 40 is little difficult.

Next group of 30 individuals are selected conveniently for doing three kinds of Aschothana. Three groups are used for the three types of Aschothana. Each group has 10 volunteers. Among these Snehana, Aschothana patients came under the age group of 30-50.

Most of the patients indicated for Snehana Aschothana are having dryness of the eye as the major presenting complaint. Increased use of mobiles and laptops as a part of online classes or jobs are the main reasons for dryness of eye among this age group. 90 % of the cases were occupied with jobs having a screen time of 8 hours or more.

Mainly Durva Ghritha is used for doing Aschothana in Dry eye at the OP level.

Ropana Aschothana indicated patients are distributed without specificity of age. Different types of cases like scleritis, episcleritis active stages of diabetic retinopathy, CNVM, and ARMD cases were selected for doing Ropana Aschothana. All these diseases have different age distributions. Therefore, no specificity is obtained for age in Ropana Aschothana. Mridweekadi arka, chandanadi Aschothana were the most commonly indicated Aschothana for these kinds of cases

Lekhana Aschothana mainly indicated above the age group of 60. Main indication of Lekhana Aschothana is cataract. Usually thriphala arka is indicated in Lekhana Aschothana at OPD. As the incidence of cataract is found more in the age group of 60 the distribution of patients are high in this age group.

Sex- sex have no role in the study. Males and females are selected randomly.

Religion – religion also have no significant role in the present study.

Domicile- Urban and rural populations are taken in the study. Healthy volunteers are selected mainly from friends, family, and colleagues without considering domicile.

In Ropana Aschothana no people obtained from urban. In the Snehana type of Aschothana, more people obtained from urban. The reasons may be the use of technologies are common in urban than in rural.

In Lekhana Aschothana, cases are more among urbans. But domicile is supposed to be not much relevant in this cateogary.

Educational and socio economic status were taken as a part of collection of general data regarding the patient. Otherwise these factors are irrelevant for the study.

Occupation- occupation is related to diseases of eye. because occupational hazards are one of the important causes of blindness. Self-employed people are more found in Snehana Aschothana as almost all the private employees need an electronic device for data management. Similarly Pensioners and home makers are more found in Lekhana Aschothana group.

Deha prakrihi- mixed features of prakrithi are obtained as a part of general assessment. Prakrithic features of eye are surveyed among volunteers separately. Eventhough expected, not much relevance is obtained for prakrithi in the study.

Manasa prakrithi – found to be an insignificant factor in the study

Analysis of **satva, satmya and ahara** were also found to be irrelevant factors as per the objectives of the study.

SECTION B CONSISTS OF A DISCUSSION ON ASCHOTHANA KRIYA KALPA

Aschothana is the foremost Kriyakalpa indicated at the early stage of a disease if the dosha vitiation is minimal. In Aschothana the liquid medicine is instilled from a height of 2A in the eyes that are kept open. Even though this is one of the prevalent Kriyakalpa, the methodology of this procedure needs more clarity while comparing classical references and actual practice.

A major issue arises with the difficulty in the practical application of classically mentioned doses of Aschothana as the conjunctival capacity can not exceed 30µL and the size of one drop is .05ml.

The second issue is regarding the site of application of medicine. Classically Kaneenaka Sandhi is mentioned but this also varies from person to person. Therefore checking the possibility of applying for medicine at Kaneenaka Sandhi in the classical dose and its effectiveness compared to the usual method should be checked.

In order to check the previous experience of applying herbal eye drops in the eyes a pilot study was conducted in the form of a survey among local communities. The survey helped to reveal certain important factors related to Aschothana as follows :

1. Procedure of doing herbal medicated solutions in the form of eyedrops is a common way of treating acute inflammatory response of the eye.
2. Commonly leave juices/ breast milk/ Kashaya/honey/cow's milk/ chandanadi yoga are used according to the condition of the patient.
3. The quantity of medicine is equal to the maximum amount of liquid that can be held in the eye.
4. There are two methodologies in practice- one is filling the eye with medicine that is squeezed directly into the eyes and spillage is prevented using fingers kept near the outer canthus of the eyes. The second method includes filling the eyes with medicine but the excess quantity that is falling out of the eye through outer canthus is not obstructed.
5. Therefore, the respondents had no certainty regarding how many number of drops of medicine instilled, 90 % of patients followed either one of the above-described methods.
6. Practice of herbal eye drops can be considered as an ancient medical practice that has changed hands for generations. And most of the time it is used as a home remedy.

The survey was useful in emphasizing the prevalence of the practice of Aschothana among common people. Compared to the current practice dose they used is high, where nowadays even in academies preferable dose is 3-4 only.

Statistical analysis was done for standardization of dose of Aschothana procedure in the following steps.

- **standardization of pichu varthi**
- **comparison of dropper bottle with Pichu varthi method**
- **Analysis of exophthalmometric values**
- **Analysis of Prakrithic features of eye**
- **Analysis of Liquid Holding Capacity of Healthy Volunteers**
- **Analysis of Aschothana at Drik Madhya and Kaneenaka**

Based on the results discussion can be done in 4 subsections

It include :

1. Patient-related factors
2. Therapy-related factors
3. Absorption of drug related factors
4. Social/economic factors

1) PATIENT-RELATED FACTORS

Patient-related factors include all contributions from the side of the patient

it include :

- **Creating awareness about the procedure**
- **Characteristic features of the eye**

- **Patient awareness**

Awareness is educating the patient about the procedure in order to avoid unnecessary complications and side effects while doing the procedure.

- **Characteristic features of eye**
    - Anatomical dimensions of the eyes

Human eyes have an oblate spheroid shape with dimensions

- Anteroposterior diameter 24 mm
- Horizontal diameter 23.5 mm
- Vertical diameter -23 mm
- Circumference – 75mm
- Volume – 6.5 ml
- Weight – 7 gm

    - Kaneenaka Sandhi and Drik Madhya

As per classics there are two sites mentioned for doing Aschothana- one is Drik Madhya according to Sarngadhara and the other is Kaneenaka Sandhi according to Susrtuha, & Vagbhata. According to modern ophthalmic pharmacokinetics, eye drops are applied over the lower area of the conjunctival sac.

The amount of liquid that can be held in the eye is dependent on the site of application of medicine. So the capacity of the eye to hold the medicine in Aschothana is different for Kaneenaka Sandhi and Drik Madhya

- Amount of exophthalmos is the linking factor of the application of medicine at Drik Madhya.

Exophthalmometry is the measurement of protrusion of the eye in the socket. while doing Aschothana at Drik Madhya it is an important factor.

The normal range of value extends from 12-21 mm.(1) The bulging can be either physiological or pathological. The range of protrusion may vary from person to person as the size and shape of the eye varies. Hertel/ LueddeI and Naugle are the common models of exophthalmometer available in the market. In this study, Luedde exophthalmometer is used.

The study include 90 volunteers and exophthalmometry were taken for all of them.

Out of 90 volunteers, 60 are healthy and among them, liquid holding capacity is checked using sterile water.

The second group is subdivided into three with each group having 10 members. This division is based on the three kinds of Aschothana. Three commonly used and easily available drugs with few side effects were selected in order to test how many drops can be held at two different locations of the eye. For Lekhana Aschothana honey , for Ropana Aschothana Mridweekadi arka and for Snehana Aschothana durva ghritha is used.

The statistical average of liquid holding capacity of healthy volunteers showed 3.35 drops are possible at the centre of eye. in Lekhana Aschothana it again decreases to 2.5. in Snehana and Ropana Aschothana it is similar to healthy volunteers , 3 and 3.4 respectively.

The reasons can be

1. high sensitivity of cornea- causes reflex blinking and watering of eyes
2. protrusion of eyeball
3. tear turn over

the average exophthalmometry value in healthy volunteers are -12.22 mm

in Lekhana Aschothana group it is 13.1. which is also normal. The deviation from healthy volunteers is 0.9 mm. Systemic reasons that can cause exophthalmos was ruled out and the reasons can be due to age-related changes.

In the group of Ropana Aschothana average value obtained is 15.3 mm and the mean difference from the normal value is 3.083. 99% of the group members of Ropana Aschothana had a normal range of values. But one patient has got an exophthalmometric value of 29 mm. which can be the possible reason behind these variations.

In Snehana Aschothana also,99 % of persons have a normal range of values but one patient had sunken eyes and the value of exophthalmometry was 11 mm. The mean value of exophthalmometry in Snehana Aschothana is 14.2 mm and the mean difference is 1.98.

Exophthalmometric values and number of drops that can be held at drik Madhya were plotted as graphs for healthy controls as well as for diseased persons.

And it is found that application of medicine at Drik Madhya, a maximum of 3-4 drops were possible including healthy volunteers. If the patient has exophthalmos, the dose further decreases and vice versa in enophthalmos.

For emphasizing the role of exophthalmometry in Aschothana few special cases having exophthalmometric values other than the normal range obtained while doing the procedure are as follows :

1. Exophthalmometric value- 29 mm B\L
   number of drops applied at Kaneenaka- 12 B/L

   Number of drops applied at Drik Madhya – 2 B/L

2. Exophthalmometric value – 31 mm in the left eye and 13 mm in the Right eye
   Number of drops applied at Drik Madhya in R eye- 2 & L eye- 4
   Number of drops applied at Kaneenaka in R eye – 12 & L eye- 14
3. Exophthalmometric value – 10 mm B\L
   Number of drops applied at Drik Madhya – 7 B/L

Number of drops applied at Kaneenaka – 14 B/L

If we analyze these findings it is evident that for applying classical dose in Aschothana , protrusion of the eye is not a relevant factor.

- Analysis of Prakrithi of eyes – Necessary while applying medicine at Kaneenaka Sandhi

As per Ayurveda natural constitution or prakrithi of each individual is different and based on the Prakriti, the feature of each part of the body is different from person to person.

while applying for medicine at Kaneenaka Sandhi, features of the eye on the basis of Prakriti can be considered as a dependent factor. But the study didn't focused in assessing prakrithi of eye and so quantitative scoring of prakrithi couldn't do.

The major factor assessed in this study was exophthalmometry on the basis of it, number of drops that can be held at drik Madhya and Kaneenaka sandhi was assessed.

2) THERAPY-RELATED FACTORS

Therapy-related factors include stepwise discussion of Aschothana Kriyakalpa.

Aschothana is done using a Pichu varthi hanging from a sukthi filled with medicine from a height of 2A.

Sukthi or Gokarna Yantra is one of the main instruments used in Panchakarma procedures like Nasya.

Figure 8.2.1- gokarna yanthra or suktthi

Pichu varthi is a wick dipped in the medicine which allows the medicinal installation in the form of drops.

The number of drops coming from a Pichu varthi is depended on

- size of varthi
- material used for making the varthi and the nature of liquid media

The size of Varthi is standardized based on obtaining a controlled flow of medicine without interruption or time delay.

First of all different kinds of materials were tried like- cotton cloth/ kora cloth/cotton & gauze.

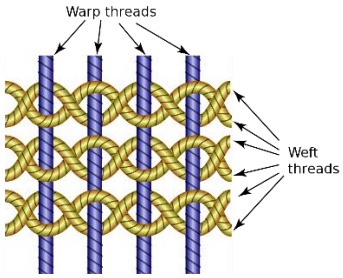
Merits and demerits of all these materials include :

Table 8.2.1 – merits and demerits of materials used for pichu varthi

MATERIAL	MERITS	DEMERITS
Cotton	1. Easily available 2. Pichu varthi shape can be made	1.The uncontrolled flow of medicine after it is completely wet 2. Medicine absorption by the material- causes drug waste
Gauze	1. Medicine absorption by the material is less 2. Easily available 3. Calculated dose as per classical references can be achieved.	-
Cotton cloth	1. Easily available	1. Medicine absorption is more by the material can cause drug wastage.

		2. Difficult to perform in highly viscous media & scanty flow of medicine is obtained
Kora cloth	1. Availability is a little difficult	1. Similar to cotton cloth, medicine absorption by the material can happen, it leads to a scanty flow of medicine in highly viscous media like honey.

Figure 8.2.2 – structure of gauze



The arrangement of threads in gauze showing the reason behind its less absorbency.

Therefore gauze is fixed as the ideal material for making pichu varthi in Aschothana as a part of this study.

Size of pichu varthi

The length of pichu varthi is fixed as 10 cm based on

- ✓ the length of the portion of sukthi where the medicinal wick is kept while doing Aschothana (which is nearly equal to 7 cm) and
- ✓ 2A or 3.5 cm for height.

So maximum length of varthi is fixed as 10 cm for this study.

The breadth of varthi is selected as a maximum of 10 cm as increasing breadth more than that of length can interrupt the free movement of liquid media kept inside the sukthi.

Few more wick or varthis are also prepared by reducing breadth by 1 cm. Thus different varthis having a breadth of 9,8,7,6,5,4,3,2 were prepared and the nature of drops falling out of each of these varthis was counted for 2 minutes.

On observation it has been found that decrease in breadth, the flow is more and it results in the flow of medicine in a stream rather than drop from. If we increase breadth very largely scanty flow of medicine is obtained, therefore medium thickness is necessary for the pichu varthi.

On decreasing the breadth more drops fell down speedily. Around 40-48 drops are obtained. This is unnecessary so decreasing breadth very largely can be avoided. If breadth is increased, the rate of flow of medicine decreases. . Among the prepared, varthis 10 * 5 cm sized varthi helped in an ideal, controlled flow of around 14 drops of medicine for the stipulated period of time.

This discussion on the role of material and size of varthi used for doing Aschothana was completed. A further step in the analysis of therapy-related factors is the various methods used for preventing spillage of medicine.

Classical compendiums of Ayurveda describe the procedure of Aschothana as instilling drops of medicine from a height of 2A into the eyes that are kept open. The doses are 8-10- 12 according to the dosha predominance. But instilling these large volumes of liquid into the ocular surface can cause an overflow of medicine. The methods that can be adopted for preventing drug overflow are not addressed in classical textbooks like Ashtanga Hridaya, Ashtanga Sangraha, Susrutha Samhitha, and Sarngadhara.

Malayalam textbooks like Chikitsa Manjari, Sarva roga chikitsa Nool, Yogamrutha, and Sahasra yoga Aschothana yogas are referred to as *akshi sechana* and *akshi sechana*. But the methodology of both of these types was not mentioned.

The same impression is observed from the comments of responders in the pilot survey where some responders said the free flow of medicine is allowed after instillation while

some others kept holding medicine in the eyes using held fingers near the outer canthus. The first method is similar to Nethra *sechana* and the second method can be considered *akshi sechana*.

Discussion on Akshi *Sechana* &*Akshi poorana*

Traditional Malayalam textbooks like yogamrutha, chikitsa manjari, and sahasra yoga described about different kinds of medicinal yogas for Aschothana. The procedure isn't specified in detail but terms like akshi *sechana* and *akshi poorana* were used accordingly. *Akshi sechana* is filling the eyes with medicine and akshi *poorana* is the method of washing the eyes with medicated liquids.

The term *akshi sechana* can be misinterpreted as seka. In seka eyes are kept closed and the medicine is poured from 4A height. But while using the term *sechana* eyes are kept open and the medicine quantity is less.

According to Acharya Susrutha, the discrimination between Seka and Aschothana was described based on dosha vitiation. Aschothana is indicated if dosha vitiation is minimal and Seka is indicated if dosha vitiation is high. Like Aschothana, there are three kinds of seka- lekhana, ropana, and snehana, but unlike Aschothana doses of Seka are not specified in our classics. Rather duration for three types is indicated as 300-400 and 600 mathra kala.

In Sarvakshi roga chikitsa of Ashtanga Hridaya seka using darvi or katamkateri is prepared in 16 part water and 1 part dari reduced to 1\8 part. The so obtained amount of Kashaya is used for seka.(2)

Therefore it is evident that unlike Aschothana Seka involves pouring medicinal liquid over the closed eye for a specified duration of time. Seka is most probably done using a large amount of diluted or semi-diluted preparations like Kashaya/ ksheera Kashaya. Duration is more important than dose.

While mentioning the word *sechana* in traditional textbooks even though the methodology is not specified, it need not be confused with Seka as the amount and nature of medicine do not match Seka's procedure.

Mostly swarasa of single drugs are indicated for doing *sechana*. The quantity is not specified still it can be taken as the amount of liquid that can be held in the open eyes. The medicine is mainly squeezed from pottery containing crushed fresh drugs especially leaves. The main examples are the use of leucus Aspera/ crepe jasmine & poovamkurunthil (Malayalam name). So *sechana* can be differentiated from Seka based on these reasons.

Another meaning of *sechana* is washing the eyes. Already Nethra kshalana or Nethra prakshalana is mentioned as a separate procedure especially as paschath karma of Anjana according to Ashtanga Hridaya. The procedure is not mentioned but in clinical practice kshalana is done like Seka but the eyes are kept open and closed alternately. It help to eliminate the discharges and remnant oushada in the eye after Anjana. The drugs are selected as per the condition of disease and climate while doing Anjana. There is no dose or duration mentioned for Nethra kshalana. So here akshi *sechana* can not be considered as Nethra kshalana. Also akshi sechana unlike Anjana explained for acute management. But Anjana is used after acute stage is over.

Hence akshi *sechana* is possibly one method of Aschothana itself and can not be considered as seka or kshalana.

Another word is *akshi poorana* can be considered as filling the eyes with medicine but the duration, as well as the method of holding, are not mentioned. In traditional practice, people use the fingers of their hands at the outer canthus for holding the medicine in their eyes. But there is no references regarding the methodology of poorana available. In tharpana pali made up of Masha or Godhuma is used around the eyes for keeping medicine in the eyes. But no such steps are mentioned under the context of *akshi poorana*

Further discussion can be done about the properties of drugs used in different kinds of Aschothana.

Among the properties of drugs pH value is the first one to be discussed as research articles regarding modern topical applications saying the optimum pH for eye drops must be equals that of tear fluid and is about 7.4. If the pH value gets outside the range of this limit which cannot be tolerated by the eyes & the patient may feel discomfort, and irritation, leading to early washout of medicine.

Balancing pH is therefore important in the case of modern topical applications.. Most of the topical applications like Chandanadi yoga, Arka preparations, and Ilaneer-kuhambu Anjana all have a pH below 7 and all the clinical pieces of evidence are saying patients using these yogas for years are still having no ocular discomfort or associated difficulties. Therefore we can say that ,pH balancing is not an important step in Ayurvedic topical applications.

The action of ayurvedic drugs cannot be completely explained on the basis of modern theories The pharmacological activity of herbal formulation is supposed to be dependent certain factors known as rasa panchaka- *rasa/ guna/ veerya/ vipaka and prabhava*.(3)

According to ayurvedic principles all dravyas are *panchamahabhoutika a*nd the pharmacological action of any dravya is determined by the composition of *panchamahabhootha* present in it. Tridosha theory and Pancha mahabhootha theory play an important role in the Pharmacokinetics of Ayurveda.

Based on these, management of any condition as per Ayurveda involves drugs having qualities that are opposite to the dosha vitiation. One of the main treatment theories as per Ayurveda is to increase the decreased properties and to decrease the increased properties.

For instance in order to tackle Kapha dosha out of the body, the drugs should have properties like rooksha (rough)/ ushna (hot)/ laghu (light)/ theekshna (powerful/ penetrating). The example can be explained in the context of Aschothana. Lekhana Aschothana is indicated in Kapha' predominant conditions of the eye. Drugs possessing these characteristics commonly known as Lekhana dravyas, (according to sarngadhara) may have pH not synchronized with that of tear constituents ie; Sarngadhara acharya saying honey/ hot water/ vacha/ yava are good examples for lekhana dravya.(4)

Among these, honey is one of the important constituent in Kriyakalpa yogas, especially for Anjana & Aschothana. The pH of honey may vary from 3.5-5.5 depending upon the source. Therefore honey is acidic in nature and it can cause ocular irritation. At the same time, honey is said to be chakshushya (good for eyes) according to Caraka, Susrutha & Vagbhata

The ocular benefits of honey have been searched by the modern research field also. The anti-bacterial anti-inflammatory wound-healing properties of honey have been utilized in multisystem disorders like ocular conditions/ CVS disorders /GIT disorders. Honey is a powerful base for topical applications like ointments, gels & emulsions. (5)So all these again emphasize the fact- pH balancing is not at all a mandatory step in topical applications.

Thus we can conclude that unlike modern theories of drug absorption many factors like pH, viscosity, solubility are fail to explain the action of drug as per ayurveda in many conditions. Ayurveda have its own theoretical explanations like thri dosha theory, pancha mahabhootha theory, rasa panchaka theory for explaining pharmacokinetics of Ayurvedic therapies and therapeutics. Even if any other modern factors are found to be unfavorable, any of the rasa panchaka can explain the mode of action of a dravya.

3) ABSORPTION OF DRUG RELATED FACTORS

Mode of action of any topical application can be divided into two sections:

Drug penetration

Drug absorption

Drug penetration

Drug penetration can occur at

Cornea

Conjunctiva

Sclera

When applied at the ocular surface, any drug penetrates these tissues depending on the physical and chemical characteristics. The basic structure of the cornea dictates the relative penetration of drugs. Effectively, the greatest barrier to drug penetration is the corneal epithelium rich in cellular membranes and is, therefore, more susceptible to penetration by lipophilic drugs.

In contrast, since the corneal stroma is largely constituted of water, drugs pass more readily through this thickest component of the cornea if they are hydrophilic.

The endothelium represents a monolayer that, once more, is lipophilic. Conjunctiva plays important roles including protection of the ocular surface, production of the tear film, and a conduit for drug clearance (depending on drug properties) into the systemic circulation. or for drug transport to the deep tissues of the eye. The conjunctiva, a moderately tight epithelium, is endowed with various transport processes for the homeostasis of ions, solutes, and water in the conjunctival surface and tear film. Compared to the cornea, the conjunctiva is less permeable for lipophilic agents. Furthermore, tight junctions of conjunctival epithelium also reduce its permeability to hydrophilic molecules.

The sclera has a similar fibrous structure as the corneal stroma but is vascularized and covered by the loose fibrous layer of the conjunctiva. The cornea and sclera are the rate-limiting barriers that block the penetration of drugs into intraocular tissues. Unlike corneal and conjunctival tissues permeability of scleral tissue is dependent on the radius of the molecules rather than the lipophilicity/hydrophilicity of the drug.

Based on the physical and chemical characteristics of different kinds of medications used in three kinds of aschothana the drug can penetrate these structures.

But drug penetration according to Ayurvedic principles have a different dimension.

In Ayurveda, rasa panchaka have got an important role. As per the conditions we can choose *rasa, guna , veerya , vipaka* of drugs that can tackle the situation of dosha vitiation in the body. For example in active bleeding stages of retina drugs or group of drugs can be chosen for doing Aschothana. In paithika abhishyanda manjishtadi seka is advised, which can be considered as one example for this.

Penetration of drug in procedures like mukha lepa, seka in retinal conditions are still not have scientific evidences but we have so many clinical evidences. Also drug applied in remote areas like vasthi karma in Nethra roga chikitsa also fail to explain how drug penetration occur in these procedures. In the same way a comparison of pharmacokinetics of Aschothana can never be correlated completely to modern topical applications. That dose not mean the procedure is uneffective.

Drug absorption

There are two possible routes of absorption of topical application are :

1. corneal route
2. Non corneal route

Corneal route involving cornea- aqueous humor- intraocular tissues

Non corneal route involving conjunctiva- sclera/choroid- retinal pigment epithelium

Two major barriers that limit the entry of medicine absorption are BAB & BRB

In the case of aschothana possible pathway of drug action is quoted as

Gatva sandhi siro ghrana mukha srothamsi bheshajam

Oordhvagaan nayane nyasthamapavarthayathe malaan

As per this opinion, naso lacrimal route is the most common pathway for drug absorption. In aschothana medicine is applied over kaneenaka sandhi and so applied medicine can easily enter the naso-lacrimal drainage system.

Nasal route of medication is very important pathway for jathruurdhvagatha vikaras, as it is already mentioned that nose is the entry point of siras.

According to Acharya Vagbhata the medicine which is administered through nasal route reach the Sringhataka marma and distributed in entire head and give very effective results in Urdhvajatrugata roga. There are three kinds of nasya- brimhana, rechana and samana. In shirovirechana the drug enters into head and causes elimination of morbid matters out of the body. In samana type drug pacifies or alleviate the vitiated doshas. In brimhana nourishment to nasa,karna,jihva and Nethra occurs.

Similarly in the case of aschothana three types are there- lekhana, snehana and ropana. In lekhana aschothana elimination of vitiated dosha out of body happens. And in ropana aschothana pacification or alleviation of the dosha and in snehana aschothana brimhana or nourishment of respective site is required.The mode of action of other topical applications like Anjana, seka can also assumed to be similar to nasya.

On the basis of these findings role of Ayurvedic topical applications can not be limited to local region only. In systemic diseases like CNS involved conditions, syncope, coma, fainting, treatment of poisioning prayoga of Anjana , nasya are mentioned. Unlike allopathic medication ayurvedic pharmacokinetics have clinical evidences rather than scientific models , therefore more specified studies are necessary in future to clarify the assumptions.

SCOCIO-ECONOMIC FACTORS

Socio economic factors include economical aspects about the procedure

Compared to all other topical applications, eyedrops are economically accepted by the patients. In literature especially traditional practice of aschothana use of easily available or economically cheap drugs are mentioned.

Social acceptance of eyedrops are more due to the fact that compared to other therapies instilling drops in the eye can be attempted by self practice. According to modern research articles the success rate of self application of medicine is found to be less compared to actual method. In case of aschothana, self application of medicine at kaneenaka can cause spillage of medicine.

Advising pichu varthi method should not be a safe method in all situations in order to avoid chances of contamination. Dropper bottle is more convenient and safe method for all age group.

By concluding Aschothana Kriyakalpa is one of the simplest and cost effective procedure beneficial in acute inflammatory conditions. The classical doses of the three kinds of Aschothana is practically possible for an eye if the medicine is instilled at inner canthus. Modern pharmacological concepts have limited role in explaining the effects of ayurvedic formulations.

SUMMARY

SUMMARY

The dissertation entitled "STANDARDIZATION OF DOSE OF ASCHOTHANA" was conducted in the Department of Salakyatantra at Government Ayurveda College, Tripunithura.

The thesis work comprises the following sections viz. Introduction, literary review, rationale and relevance, methodology, results, and discussion. The present section is dealing with the summary and conclusion.

The first section i.e. Introduction is the preface of the dissertation which includes the details regarding Kriyakalpas with special emphasis on Aschothana and its classical reviews.

A review of literature is the next section of this thesis work which includes 8 chapters. Viz. Anatomical and physiological aspects of the ocular surface, the concept of Nethra sareera as per Ayurvedic Classics, details about ocular barriers, different methods of ocular drug delivery, analysis of Kriyakalpas with special reference to Aschothana, details about exophthalmometry , characteristics of Prakriti, &details about standardization.

In the first chapter anatomical aspects of the structures that contribute ocular surface are discussed in detail. It includes cornea, sclera, conjunctiva, eyelids & tear film.

The second chapter deals with the Ayurvedic aspects of the Anatomy of the eye. Features of size and shape as per classical references were included. Also panchabhouthikathva of structures related to the ocular surface of eye, mandala related to the ocular surface, sandhis related to the ocular surface and Nethra patalas are discussed in detail.

The third chapter is dealing with the detailed anatomy of ocular barriers of eye. Anatomical barriers like BAB, corneal epithelium, conjunctival and scleral barriers are included. In physiological barriers – tear turnover, reflex blinking, efflux pumps and naso lacrimal drainage were discussed separately.

Chapter four deals with ocular drug delivery, pre measures to improve the bioavailability of topical applications, limitations of oral medicine in ocular diseases management as per modern pharmacokinetics, prodrug strategies and nanotechnology-based drug delivery

systems. Ayurvedic concepts of bioavailability, bioavailability enhancers and the scope of using synthetic polymers from natural substances are described in the last section.

A detailed description of Kriyakalpa with special mention on Aschothana is included in the next chapter. Each and every aspects of Aschothana with references of Aschothana-related descriptions from available classical text books were written.

In chapter five exophthalmometry and in chapter six concepts of prakrithi were discussed. In the last chapter standardization and scope of standardization in Ayurveda were included. A comparison of the term Bindu according to different contexts was also included at the end of this chapter.

The next section explains the rationale and relevance of the study.

In the methodology, the focus was given to explaining the core area of the study which includes objectives, materials, and methods, details regarding standardization procedure of pichu varthi, the liquid holding capacity of healthy volunteer, measurement of exophthalmometry standardization of dose of aschothana, inclusion and exclusion criteria of patients, recording data of patient and statistical analysis of collected data were included.

The heading Results comprises observation, analysis, and interpretation of the study. Two sections were given. In section A, the demographic data of patients registered in case proforma was observed and analyzed accordingly, interpretation was made to find out the relevance of those points in the liquid holding capacity of the eye.

In section B the data related to standardization of dose of the three kinds of Aschothana were done. For that standardization of pichu varthi, relation between exophthalmometric values with liquid holding capacity at drik Madhya and Kaneenaka sandhi were tested. The number of doses possible at healthy volunteers, Lekhana Aschothana , Ropana Aschothana and in Snehana Aschothana were checked using sterile water, honey, Mridweekadi arka and durva ghritha respectively.

The average value of exophthalmometry obtained are :

in healthy volunteers is 12.22 mm

in Lekhana Aschothana – 13.1 mm

Ropana Aschothana 15.3 mm and in Snehana Aschothana 14.3 mm

The average possible number of drops in healthy volunteers at Drik Madhya and Kaneenaka sandhi are respectively are 7.5 and 3.3 similarly in Lekhana Aschothana number of drops possible at drik Madhya and Kaneenaka 2.5 and 4.6 respectively. In Ropana Aschothana number of drops could be possible at drik Madhya and Kaneenaka sandhi are 3 and 7.7 respectively. In Snehana Aschothana the number of drops possible at drik Madhya and Kaneenaka are 3.4 and 5.3 respectively.

Discussion includes logical explanation and elaboration about all the areas related with the present dissertation.

The summary and conclusion is the final part of the study which deals with an outline of the entire work on the basis of available ayurvedic and modern literature and the data of the present study.

The dissertation is summarized as follows:

The study includes 90 volunteers, grouped into two. One group consists of 60 healthy volunteers and the second group consists of 30 diseased volunteers. The second group is equally divided into three subgroups for standardizing the dose of three kinds of Aschothana. Standardized pichu varthi is used for doing aschothana. For standardization different kinds of material and sizes of varthi or wicks were tried. In the end comparison - of pichu varthi with eyedropper bottle is done as availability, and safety from contamination are less in the latter. Three kinds of Aschothana were done using this varthi at two different locations as per classical references and a comparison was done. Final observations related to all these findings were tabulated, and statistically tested and the significance of doing Aschothana at Kaneenaka Sandhi was found to be more convenient for the practice of Aschothana close to classically mentioned drops. Relation between exophthalmometry and number of drops applied at Kaneenaka sandhi have negligible relation and exophthalmometry and number of drops applied at drik Madhya have a negative correlation according to spearman correlation co efficient

CONCLUSION

CONCLUSION

The conclusions are drawn as per proper assessment, interpretation, and observations.

The main aim of the study is to standardize the doses of three kinds of Aschothana as the clinical practice of this Kriyakalpa follows a dose range in the limit of a maximum of 3-4 drops only.

Modern research articles regarding the topical applications of the eye especially eyedrops accentuate the clinical practice because conjunctival capacity cannot hold even one drop of medicine as the size of them are 30µL and 0.05ml respectively. But ancestors attempted some modifications in the procedure in order to accommodate large doses of medicine in the eyes. The possibility of applying indicated doses of Aschothana as per classical references should be checked along with the role of some influencing factors like exophthalmometry, size, and shape of eyes.

A standardized-sized Pichu varthi is used for instilling medicines in the eyes. Based on these findings calculation, tabulation, and interpretation of necessary data as per methodology were done statistically. The Chi-square test and spearman correlation coefficient test were used to statistical analysis of the data.

And the results showed a classical dose of Aschothana can be applied in the eyes if the medicine is dripped at Kaneenaka Sandhi and only 3-4 drops can be applied if the medicine is dripped at Drik Madhya. As per the tests, exophthalmometry is negatively correlated to Aschothana at drik Madhya while exophthalmometry at Kaneenaka has not much significant relation according to the Spearman correlation coefficient

In order to do the correct practice of Aschothana in the future and comparison of pichu varthi with eyedropper is also done since negligible differences are obtained dropper bottle can be advised in OPD practice of Aschothana.

LIMITATIONS & SUGGESTIONS OF THE STUDY

1. Calculation of dose could be done based on site of application and exophthalmometric values only.
2. Role of Prakriti couldn't be checked.
3. The standardization of Aschothana dravyas couldn't do.
4. Effectiveness of applying classical dose and clinically practiced dose can be checked using a true clinical trial.
5. On the basis of exophthalmometry category-wise comparison and difference in dose obtained for exophthalmos, enophthalmos couldn't be checked.
6. Another study can be conducted, in order to find out all influencing factors for the effective dose of Achothana in pathological conditions for an expected outcome
7. Study for absolute dose of Aschothana

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DISCUSSION

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ANNEXURE

ANNEXURE 1

CASE PROFORMA FOR RESEARCH MS (Ay)

DEPARTMENT OF SALAKYATANTRA, GOVT. AYURVEDA

COLLEGE HOSPITAL TRIPUNITHURA

TITLE: STANDARDIZATION OF DOSE OF ASCHOTHANA

Name of scholar: Jesna Gopinath

Guide: Dr. Sreeja Sukesan MD (Ay) PhD

Period of study: 18 months

PARTICULARS OF THE PATIENT

Name :

Serial no :

Age :

O.P No :

Sex :

I.P No :

Address & phone no :

D.O.A :

D.O.D :

Occupation :

Religion : Hindu/ Muslim/ Christian/ Others

Marital status : Married/ Unmarried

Domicile : Urban / rural

Education :

Socio- economic status : P / LM / UM/ R

PRESENTING COMPLAINTS AND DURATION

Chief complaints with duration:

HISTORY OF PRESENTING COMPLAINTS :

HISTORY OF PAST ILLNESS :

TREATMENT HISTORY:

FAMILY HISTORY:

PERSONAL HISTORY:

Habits : Exercise :

Diet : Appetite:

Bowel : Micturition :

Sleep :

ROGI PAREEKSHA:

GENERAL EXAMINATION:

Pulse : /min Blood pressure : / mm of Hg

Temperature : ^{0}F Respiratory rate : /min

Heart rate : /min

Height : Weight :

Built : Pallor : present/absent

Cyanosis :

SYSTEMIC EXAMINATIONS:

Cardio vascular system :

Respiratory system :

Digestive system :

Genito urinary system :

Nervous system :

PHYSICAL EXAMINATION OF EYE: RIGHT LEFT

EXAMINATION OF EYE :

1.Eye ball

Position	normal/Symmetrical
	Abducted/Adducted
	Exopthaimos/Enopthalmos
Visual axis	Normal
	Deviated
Size	Normal
	Microphthalmos/ Macrophthalmos/ Pthysis bulbi
Movements	normal
	Abnormal/ Restricted

2.Eye brows

	Normal
	Abnormal

3.Eye lids

Position-upper lid	Normal
	Ptosis
	Lid retraction
Position-lower lid	Normal
	Lagging
Movements	Normal
	Increased blinking
	Reduced blinking
	Lagopthalmos

Appearance	Normal
	Redness
	Swelling
	Pigmentation
Lid margins	Normal
	Thickened
	Ectropion
	Entropion
Eyelashes	Normal
	Trachiasis
	Distichiasis
	Madarosis
	Poliosis
	Parasites
	Matting
Palpebral fissure	Normal
	Narrow
	Wide

4.Lacrimal apparatus

Lacrimal puncta	Open
	Stenosed
	Everted
	Inflammed
Lacrimal sac area	Normal
	Redness

	Swelling
	Fistula
Lacrimal passage	Patent
	Non patent
Level of obstruction	Inferior canaliculi
(if non patent)	Superior canaliculi
	Common canaliculus
	Nasolacrimal duct
Regurgitation test	No discharge
	Watery discharge
	Mucoid discharge
	Purulent discharge
	Other

5.Conjunctiva

Bulbar conjunctiva	Normal
	Lustreless
	Congested
	Discharge
	Chemosis
	Pterygium
	Bitot’s spots
Palpebral conjunctiva	Normal
	Papillae
	Follicles
	Concretions
	Scarring

	Congestion
Fornix	Normal/congested

6.Cornea

Size	Normal
	Micro cornea
	Megalo cornea
Shape	Normal
	Flat
	Conical
	Globular
Surface	Smooth and regular
	Corneal ulcer
	Corneal abrasions
	Corneal opacity
Placido’s disc image	Regular
	Distorted
Transparency	Transparent
	Hazy
	Opacity
Corneal sensation	Good/brisk
	Diminished
	Absent

7.Anterior chamber

Depth	Normal
	Shallow
	Deep
Abnormal contents	Present
	Absent

8.Iris

Colour	Normal
	Abnormal
Pattern	Normal
	Abnormal
Others	Iridodonesis
	Synechia
	Vascularisation

9. Pupil

Size	Normal
	Miosis
	Mydriasis
Shape	Circular
	Irregular
Colour	
Position	
Pupillary reaction	Good
	Sluggish
	Absent

9. Lens

Colour	Transparent
	Greyish white
	Pearly white
	Milky white
Position	Normal
	Subluxation
	Dislocation

11. colour vision

12. Intra ocular pressure

FUNCTIONAL TESTS

1) VISUAL ACUITY
   - Distant vision
   - With pinhole
   - Near vision
   - BCVA
   - Correction if needed:

2)SLIT LAMP EXAMINATION

3)FUNDUS EXAMINATION

ASHTA STHANA PAREEKSHA:

Nadi -	Mootra -
Malam -	Jihwa -
Shabdam-	Sparsham-
Drik -	Akruti -

DASHA VIDHA PAREEKSHA:

1.Dooshyam:

2.Desam:

3. Balam:

Roga bala; - pravara / madhyama / avara

Rogi bala:- uthama / madhyama / alpa

4.Kalam:

kshanadi kalam

Vyadhyavastha kala

5.Analam: mandha / theekshna / vishama / sama

6.Prakruti: VP/ PK / VK / SAMA Prakruti

7.Vaya: bala / madhyama / jeerna

8.Satwa: pravara / madhyama / avara

9.Satmya: sarva rasa/ vyamisra/ eka rasa

10.Ahara :

i)Abhyavaharana sakthi

ii)Jarana Sakthi

PRAKRITHI PAREEKSHA OF EYES :

VATA	PITHA	KAPHA
Small	Medium	Wide/wider
Dull	Penetrating look	Gentle look
Offwhite	Red tinged	White

ROGA PAREEKSHA:

Nidana:

Poorvarupa:

Roopa:

Upasaya:

SAMPRAPTI GATAKAS:

Dosha:

Dushya:

Srotas:

Roga marga:

Vyadhi swabhava: Asukari / chirakari

DIAGNOSIS OF THE CASE :

TYPE OF ASCHOTHANA USED :

AMOUNT OF ASCHOTHANA THAT CAN BE HELD IN THE EYES :

(at Kaneenaka Sandhi/ at Drik Madhya) in drops

ANNEXURE -2

CONSENT FORM

CONSENT FORM

I…… …… ……exercise my free power of choice by giving you complete consent to be included as a subject in the trial ‘ STANDARDIZATION OF DOSE OF ASCHOTHANA’ conducted in the department of Salakyatantra,Govt. Ayurveda College Hospital,Tripunithura. I have been informed to my satisfaction by the attending doctor about the purpose of clinical trial, nature of procedure, follow up and complication. I am also aware of my right to opt out of the trial at any time during the course of the trial without having to give the reason for doing so.

Date Signature of patient/Guardian

Place: Name :

സമ്മതപത്രം

ഈ സമ്മതപത്രത്തിൽ ഒപ്പിട്ടിരിക്കുന്ന ഞാൻ എന്റെ പൂർണ സമ്മതത്തോ ടുകൂടി ഈ ഗവേഷണ പരിപാടിയിൽ പങ്കെടുക്കുന്നതാണ്. ഇതേ പറ്റിയുള്ള പൂർണ്ണ വിവരങ്ങൾ എന്റെ സ്വന്തം ഭാഷയിൽ എന്നെ ധരിപ്പിച്ചിട്ടുള്ളതാകുന്നു. ഈ ഗവേഷണത്തിന്റെ ഏതു ഘട്ടത്തിലും ഇതിൽ നിന്നും പിന്മാറാനുള്ള സ്വാതന്ത്രം ഉണ്ടായിരിക്കുന്നതാണ്. ഈ സമ്മതപത്രത്തിലെ ഒപ്പ് ഈ ഗവേഷണ പരിപാടിയെ കുറിച്ചുള്ള പൂർണ്ണ വിവരങ്ങൾ മനസിലാക്കി എന്നതിനും ഇതിന്റെ ഭാഗമായുള്ള രോഗ പരീക്ഷയിൽ പങ്കെടുക്കുന്നതിന് സമ്മതമാണ് എന്നതിനും സൂചനയാണ്.

ഗവേഷകന്റെ ഒപ്പ്

സ്ഥലം

രോഗിയുടെ പേര്

ഒപ്പ്/വിരലടയാളം

NAME AND SIGNATURE OF PG SCHOLAR : Dr. Jesna Gopinath

NAME AND SIGNATURE OF GUIDE : Dr. Sreeja Sukesan MD(Ay) PhD

MASTER CHARTS

SL NUM	AGE	SEX	ADDRESS	RELIGION	DOMICILE
1	25	F	PUTHIYAKAV	CHRISTHIAN	RURAL
2	23	F	PUTHIYAKAV	HINDU	RURAL
3	29	F	PUTHIYAKAV	HINDU	RURAL
4	26	F	PUTHIYAKAV	HINDU	RURAL
5	32	F	PUTHIYAKAV	HINDU	RURAL
6	27	F	PUTHIYAKAV	MUSLIM	RURAL
7	26	F	PUTHIYAKAV	MUSLIM	RURAL
8	25	F	PUTHIYAKAV	HINDU	RURAL
9	33	F	PUTHIYAKAV	HINDU	RURAL
10	31	F	PUTHIYAKAV	HINDU	RURAL
11	25	F	PUTHIYAKAV	HINDU	RURAL
12	25	F	PUTHIYAKAV	CHRISTHIAN	RURAL
13	24	F	PUTHIYAKAV	HINDU	RURAL
14	26	F	PUTHIYAKAV	HINDU	URBAN
15	18	M	NORTH PARAVOOR	HINDU	URBAN
16	31	M	ERAMALLOOR	HINDU	RURAL
17	53	M	NORTH PARAVOOR	HINDU	URBAN
18	47	F	NORTH PARAVOOR	HINDU	URBAN
19	39	F	THURAVOOR	HINDU	RURAL
20	36	F	KOTTAYAM	HINDU	URBAN
21	19	M	ERAMALLOOR	HINDU	RURAL
22	21	M	ERAMALLOOR	HINDU	RURAL
23	44	F	ERAMALLOOR	HINDU	RURAL
24	49	M	ERAMALLOOR	HINDU	RURAL
25	34	M	ERAMALLOOR	MUSLIM	URBAN
26	24	F	ERAMALLOOR	MUSLIM	URBAN
27	18	F	CHERTHALA	HINDU	URBAN
28	26	F	THURAVOOR	HINDU	RURAL
29	29	M	THURAVOOR	HINDU	URBAN
30	18	F	CHERTHALA	HINDU	URBAN
31	20	M	CHERTHALA	HINDU	URBAN
32	21	M	CHERTHALA	HINDU	RURAL
33	25	F	CHERTHALA	HINDU	RURAL
34	22	M	CHERTHALA	HINDU	RURAL
35	29	F	BANGLOOR	HINDU	URBAN
36	30	F	THIRUVANTHAPURAM	HINDU	URBAN
37	30	F	THIRUVANTHAPURAM	HINDU	URBAN
38	25	M	PUTHIYAKAV	HINDU	RURAL
39	42	F	ALAPPUZHA	HINDU	URBAN
40	43	F	ALAPPUZHA	HINDU	RURAL
41	36	F	CHERTHALA	HINDU	RURAL
42	24	F	PUTHIYAKAV	HINDU	RURAL

43	33	M	ERAMALLOOR	HINDU	URBAN
44	38	M	KOTHAMANGALAM	HINDU	URBAN
45	43	F	CHERTHALA	HINDU	RURAL
46	48	M	ERAMALLOOR	HINDU	RURAL
47	40	F	ERAMALLOOR	HINDU	RURAL
48	29	M	CHERTHALA	HINDU	RURAL
49	24	F	CHERTHALA	HINDU	URBAN
50	25	F	PUTHIYAKAV	HINDU	RURAL
51	24	M	PUTHIYAKAV	HINDU	RURAL
52	25	M	PUTHIYAKAV	CHRISTHIAN	RURAL
53	25	F	PUTHIYAKAV	MUSLIM	RURAL
54	28	M	ALUVA	HINDU	URBAN
55	29	M	ALUVA	CHRISTHIAN	URBAN
56	32	M	ALUVA	HINDU	URBAN
57	55	M	ALUVA	MUSLIM	URBAN
58	31	M	ALUVA	CHRISTHIAN	URBAN
59	58	M	ALUVA	HINDU	URBAN
60	34	M	ALUVA	HINDU	URBAN
61	56	F	ELOOR	CHRISTHIAN	URBAN
62	53	M	KOTTAYAM	HINDU	RURAL
63	76	F	EDAKOCHI	HINDU	RURAL
64	63	M	ERAMALLOOR	HINDU	RURAL
65	58	F	MARADU	HINDU	URBAN
66	60	F	PUTHIYAKAV	HINDU	RURAL
67	67	F	CHERTHALA	HINDU	RURAL
68	66	M	KOTTAYAM	HINDU	RURAL
69	73	F	CHERTHALA	HINDU	RURAL
70	50	M	CHERTHALA	HINDU	RURAL
71	23	F	KOTTAYAM	HINDU	RURAL
72	58	M	ALUVA	CHRISTHIAN	RURAL
73	58	M	KOTTAYAM	HINDU	RURAL
74	63	M	CHERAY	HINDU	RURAL
75	53	M	KOTTAYAM	HINDU	RURAL
76	61	M	PUTHIYAKAV	HINDU	RURAL
77	44	F	THIRUVANIYOOR	HINDU	RURAL
78	43	F	EROOR	HINDU	RURAL
79	22	F	CHERTHALA	HINDU	RURAL
80	14	F	THIRUVAMKULAM	HINDU	RURAL
81	28	F	KAKKANADU	CHRISTHIAN	URBAN
82	44	F	THIRUVANIYOOR	HINDU	RURAL
83	43	F	ALUVA	MUSLIM	URBAN
84	32	F	PUTHIYAKAV	HINDU	RURAL
85	24	F	PUTHIYAKAV	MUSLIM	RURAL
86	26	M	THIRUVAMKULAM	HINDU	RURAL
87	39	M	THIRUVAMKULAM	HINDU	RURAL
88	42	F	CHERTHALA	HINDU	RURAL
89	40	M	CHERTHALA	HINDU	RURAL
90	28	M	KAKKANADU	CHRISTHIAN	URBAN

SOCIO ECONOMIC STATUS	EDUCATION	OCCUPATION
UPPER MIDDLE CLASS	GRADUATION	STUDENT
POOR	GRADUATION	NURSE
POOR	GRADUATION	NURSE
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	POST GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
POOR	PLUS TWO	STUDENT
UPPER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
UPPER MIDDLE CLASS	GRADUATION	BUSINESS
UPPER MIDDLE CLASS	GRADUATION	HOME MAKER
LOWER MIDDLE CLASS	POST GRADUATION	HOME MAKER
UPPER MIDDLE CLASS	POST GRADUATION	GOVERNMENT EMPLOYEE
RICH	TENTH	STUDENT
RICH	GRADUATION	STUDENT
RICH	GRADUATION	HOME MAKER
RICH	GRADUATION	BUSINESS
UPPER MIDDLE CLASS	GRADUATION	BUSINESS
UPPER MIDDLE CLASS	GRADUATION	HOME MAKER
RICH	HIGH SCHOOL	STUDENT
RICH	POST GRADUATION	STUDENT
RICH	GRADUATION	BANK EMPLOYEE
RICH	TENTH	STUDENT
RICH	GRADUATION	STUDENT
LOWER MIDDLE CLASS	GRADUATION	STUDENT
LOWER MIDDLE CLASS	POST GRADUATION	STUDENT
LOWER MIDDLE CLASS	PLUS TWO	STUDENT
RICH	GRADUATION	HOME MAKER
UPPER MIDDLE CLASS	GRADUATION	HOME MAKER
RICH	GRADUATION	HOME MAKER
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	POST GRADUATION	GOVERNMENT EMPLOYEE
UPPER MIDDLE CLASS	POST GRADUATION	GOVERNMENT EMPLOYEE
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
RICH	GRADUATION	BUSINESS
RICH	POST GRADUATION	PRIVATE EMPLOYEE
LOWER MIDDLE CLASS	GRADUATION	BUSINESS
RICH	GRADUATION	BUSINESS

RICH	POST GRADUATION	TEACHER
UPPER MIDDLE CLASS	GRADUATION	BUSINESS
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	STUDENT
LOWER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
LOWER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
LOWER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
LOWER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
RICH	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
UPPER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
UPPER MIDDLE CLASS	GRADUATION	CENTRAL GOVERNMENT EMPLOYEE
UPPER MIDDLE CLASS	GRADUATION	HOME MAKER
LOWER MIDDLE CLASS	TENTH	COOLIE
UPPER MIDDLE CLASS	GRADUATION	RETIRED NURSE
UPPER MIDDLE CLASS	TENTH	RETIRED
UPPER MIDDLE CLASS	TENTH	HOME MAKER
LOWER MIDDLE CLASS	PREE DEGREE	HOME MAKER
LOWER MIDDLE CLASS	PREE DEGREE	HOME MAKER
UPPER MIDDLE CLASS	POST GRADUATION	RETIRED GOVERNMENT EMPLOYEE
RICH	GRADUATION	RETIRED TEACHER
RICH	POST GRADUATION	TEACHER
LOWER MIDDLE CLASS	PLUS TWO	HOME MAKER
UPPER MIDDLE CLASS	GRADUATION	BUSINESS
LOWER MIDDLE CLASS	GRADUATION	PRIVATE EMPLOYEE
POOR	BASIC	COOLIE
LOWER MIDDLE CLASS	TENTH	COOLIE
LOWER MIDDLE CLASS	TENTH	COOLIE
LOWER MIDDLE CLASS	PREE DEGREE	HOME MAKER
LOWER MIDDLE CLASS	PREE DEGREE	HOME MAKER
LOWER MIDDLE CLASS	GRADUATION	HOME MAKER
LOWER MIDDLE CLASS	HIGH SCHOOL	STUDENT
RICH	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	HOME MAKER
RICH	GRADUATION	HOME MAKER
UPPER MIDDLE CLASS	GRADUATION	PRIVATE EMPLOYEE
RICH	GRADUATION	STUDENT
UPPER MIDDLE CLASS	GRADUATION	PRIVATE EMPLOYEE
LOWER MIDDLE CLASS	GRADUATION	PRIVATE EMPLOYEE
RICH	POST GRADUATION	TEACHER

UPPER MIDDLE CLASS	GRADUATION	PRIVATE EMPLOYEE
UPPER MIDDLE CLASS	POST GRADUATION	PRIVATE EMPLOYEE

DEHA PRAKRITHI	MANASA PRAKRITHI	SATVA	SATMYAM	AHARA
P- K predominant	satvika	Madhyama	pravara	mixed
V-K predominant	tamasika	avara	pravara	mixed
k-v predominance	satvika	Madhyama	madhyama	mixed
K-P predominant	rajasika	Madhyama	madhyama	mixed
V-K predominant	satvika	Madhyama	pravara	mixed
P- K predominant	satvika	pravara	madhyama	mixed
V-K predominant	satvika	Madhyama	madhyama	mixed
V-K predominant	satvika	pravara	avara	mixed
K-P predominant	satvika	pravara	pravara	mixed
V-P predominant	satvika	Madhyama	madhyama	mixed
k-v predominance	rajasika	Madhyama	madhyama	mixed
k-v predominance	rajasika	pravara	pravara	mixed
K-P predominant	satvika	Madhyama	madhyama	vegetarian
V-K predominant	satvika	pravara	madhyama	mixed
V-P predominant	rajasika	pravara	madhyama	mixed
V-P predominant	rajasika	Madhyama	madhyama	mixed
V-K predominant	satvika	pravara	madhyama	mixed
K-P predominant	rajasika	Madhyama	madhyama	mixed
V-P predominant	tamasika	avara	madhyama	mixed
V-P predominant	rajasika	pravara	madhyama	mixed
V-K predominant	satvika	pravara	madhyama	mixed
V-K predominant	satvika	Madhyama	madhyama	mixed
K-P predominant	rajasika	avara	madhyama	mixed
V-P predominant	rajasika	pravara	madhyama	mixed
V-P predominant	satvika	Madhyama	madhyama	mixed
P-K predominant	satvika	Madhyama	pravara	mixed
V-P predominant	rajasika	Madhyama	pravara	mixed
K-P predominant	tamasika	Madhyama	madhyama	mixed
V-P predominant	satvika	Madhyama	madhyama	mixed
k-v predominance	rajasika	pravara	pravara	mixed
V-P predominant	satvika	Madhyama	avara	mixed
K-P predominant	tamasika	avara	madhyama	mixed
V-K predominant	tamasika	avara	madhyama	mixed
K-P predominant	tamasika	avara	madhyama	mixed
V-P predominant	rajasika	Madhyama	pravara	mixed
K-P predominant	satvika	Madhyama	prm	mixed
K-P predominant	satvika	Madhyama	madhyama	mixed
k-v predominance	satvika	pravara	madhyama	mixed
V-P predominant	tamasika	avara	pr	mixed
V-P predominant	rajasika	avara	madhyama	mixed
P-K predominant	tamasika	pravara	madhyama	mixed
P-K predominant	satvika	Madhyama	pravara	mixed

V-P predominant	rajasika	Madhyama	madhyama	mixed
V-K predominant	satvika	Madhyama	madhyama	mixed
V-K predominant	tamasika	avara	madhyama	mixed
K-P predominant	rajasika	pravara	avara	mixed
V-K predominant	tamasika	pravara	avara	mixed
V-P predominant	rajasika	Madhyama	madhyama	mixed
P-K predominant	rajasika	Madhyama	madhyama	mixed
K-P predominant	satvika	Madhyama	madhyama	mixed
P-K predominant	satvika	Madhyama	pravara	mixed
K-P predominant	satvika	Madhyama	pravara	mixed
P-K predominant	satvika	Madhyama	madhyama	mixed
K-P predominant	rajasika	pravara	madhyama	mixed
V-P predominant	tamasika	pravara	madhyama	mixed
V-K predominant	rajasika	pravara	avara	mixed
P-K predominant	satvika	Madhyama	avara	mixed
V-P predominant	satvika	Madhyama	pravara	mixed
K-P predominant	rajasika	Madhyama	madhyama	mixed
V-P predominant	tamasika	avara	madhyama	vegetarian
V-K predominant	rajasika	pravara	madhyama	vegetarian
K-P predominant	tamasika	avara	madhyama	mixed
V-P predominant	satvika	Madhyama	pravara	mixed
V-K predominant	satvika	Madhyama	madhyama	vegetarian
P-v predomimant	satvika	pravara	madhyama	vegetarian
K-P predominant	rajasika	avara	madhyama	mixed
P-K predominant	tamasika	Madhyama	avara	mixed
k-v predominance	rajasika	Madhyama	pravara	mixed
V-K predominant	rajasika	avara	madhyama	mixed
V-P predominant	tamasika	pravara	madhyama	mixed
P-K predominant	satvika	Madhyama	madhyama	mixed
k-v predominance	satvika	Madhyama	pravara	vegetarian
V-P predominant	satvika	pravara	madhyama	mixed
P-K predominant	rajasika	avara	madhyama	mixed
P-v predomimant	satvika	pravara	madhyama	mixed
K-P predominant	rajasika	avara	avara	mixed
K-P predominant	satvika	Madhyama	avara	vegetarian
V-K predominant	rajasika	Madhyama	madhyama	vegetarian
P-V predomimant	rajasika	avara	madhyama	vegetarian
P-K predominant	satvika	avara	pravara	vegetarian
V-K predominant	satvika	pravara	madhyama	vegetarian
K-P predominant	satvika	Madhyama	madhyama	mixed
V-P predominant	rajasika	avara	pravara	mixed
	tamasika	Madhyama	avara	mixed
	rajasika	Madhyama	madhyama	mixed
	rajasika	Madhyama	pravara	mixed
V-K predominant	rajasika	avara	madhyama	mixed
K-P predominant	satvika	avara	madhyama	mixed
P-v predomimant	satvika	avara	madhyama	mixed
V-P predominant	tamasika	pravara	madhyama	mixed

SL NUM	AGE	SEX	EXOPHTHALMOMETRY
1	56	F	13
2	53	M	16
3	76	F	11
4	63	M	12
5	58	F	13
6	60	F	14
7	67	F	13
8	66	M	12
9	73	F	13
10	50	M	14

LIQUID HOLDING CAPACITY- KANEENAKA SANDHI	LIQUID HOLDING CAPACITY- DRIK MADHYA
6	4
4	2
4	2
5	3
4	2
5	3
4	2
4	2
5	2
5	3

SL NUM	AGE	SEX	EXOPHTHALMOMETRY- in mm
1	23	F	15
2	58	M	26 mm in right and 29 mm in left
3	58	M	16
4	63	M	14
5	53	M	11
6	61	M	13
7	44	F	13
8	43	F	16
9	22	F	15
10	14	F	14

LIQUID HOLDING CAPACITY- KANEENAKA SANDHI	LIQUID HOLDING CAPACITY- DRIK MADHYA
8	4
10	2
8	4
10	3
6	3
8	3
6	3

				5	2
				8	3
				8	3

SL NUM	AGE	SEX	EXOPHTHALMOMETRY-in mm
1	28	F	16
2	44	F	15
3	43	F	14
4	32	F	13
5	24	F	16
6	26	M	11
7	39	M	14 in Right eye 16
8	42	F	14
9	40	M	16
10	28	M	13

LIQUID HOLDING CAPACITY- KANEENAKA SANDHI	LIQUID HOLDING CAPACITY - DRIK MADHYA
5	3
6	4
6	4
6	3
5	3
6	3
3 drops in left eye 2 drops in right eye	5 drops in left eye 6 drops in right eye
5	3
5	2
6	3

ACKNOWLEDGEMENT

ACKNOWLEDGEMENT

At this moment of successful completion of my dissertation work, I offer my salutations to the Almighty for having bestowed upon me good health and well being which was inevitable to achieve this milestone of my life.

My heart fills with gratitude towards many who have been encouraging and supporting me throughout this journey.

It is my privilege to express my deep sense of gratitude to my teacher and guide Dr. Sreeja Sukesan MD (Ay) Ph.D, Professor and HOD, Salakyatantra, Govt. Ayurveda College, Thripunithura for valuable guidance, immense inspiration suggestions, and constant encouragement throughout this work.

I found my words inadequate in expressing a deep sense of gratitude to Dr. Jeeja Sasi MD (Ay) MS (Ay), Associate Professor, Salakyatantra, Govt. Ayurveda College, Tripunithura & Dr. Mithra Das M ,MS (Ay), Assistant Professor Dept. of Salakyatantra, Govt. Ayurveda College, Tripunithura.

I extend my gratitude to Dr. T. D. Sreekumar MD (Ay), Principal, Govt. Ayurveda College, Tripunithura for providing all the facilities in the college for the completion of this work.

I felt short of words to extend my gratitude and love towards my supportive, affectionate batchmates Dr. Sudheesh K.P, Dr. Sandhya K , Dr. Muhammad Nizzam, Dr. Divya C S & Dr. Fathimath Naseeha. My completion of this thesis work couldn’t have been accomplished without their support.

I do solicit my generous gratitude to my seniors Dr.Lincy C.M, Dr. Resmi S & Dr. Arunima

With gratitude I summon up the assistance provided to me by my most lovely juniors

Dr. Fasna ,Dr. Gargi Mohan, Dr. Sravya , Dr. Anju, Dr. Munavara, Dr. Aryalekshmi, Dr. Amritha , Dr. Sreedevi, Dr. Nikhila, Dr. Harsha A, Dr. Harsha Bhuriya, Dr. Ajeesh, Dr.Rajalekshmi, Dr. Neethu Thomas, Dr. Pooja Kishore & Dr . Pooja Jayaprasad.

I extend my gratitude to all the staff in the Central Library, Govt. Ayurveda College, Tripunithura, & Vee vees printers for publishing this work as a book. I take this opportunity to thank all patients who cooperated with me wholeheartedly throughout the study.

I must express my very profound gratitude to my parents for providing me with unfailing support and continuous encouragement during the process of researching and writing the thesis.

It is beyond the reach of my language to oblige my bellowed husband Amjith K Mohan who like a constant driving force and great motivation for me without his support, the study wouldn't have been possible. I am indebted to him for his patience and moral support also I am remembering the love and affection of our kid Navamy K Amjith

Last but not least my humble thanks to my patients, without whom this work would not have been completed at all. I extend my sense of gratitude to each and everyone who directly helped me in the accomplishment of this venture. I beg forgiveness for my venial error and extend my gratitude to all listed and unlisted ones.

Name : Jesna Gopinath

ABBREVIATIONS

AH-Astanga Hrdaya

AS-Astanga Samgraha

BP-Bhavaprakasha

SA- Srngadhara samhitha

SU- Susrutha samhitha

KP-Kapha pitha

KV-Kapha vata

PV-Pitha vata

PK-Pitha kapha