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Review Article

REVIEW OF *ANJANA* (CORRYLIUM) PROCEDURE AND ITS PROBABLE MODE OF ACTION

Kankanan Gamage Surangi[1*], Shamsa Fiaz[2], Sahoo Prasanta Kumar[1]
*[1]MS Scholar, [2]HOD, Department of Shalakya Tantra, National Institute of Ayurveda, Jaipur, Rajasthan, India,

ABSTRACT

Shalakya Tantra is one of the eight specialties of *Ashtanga Ayurveda* which deals with diseases occur above the clavicle specially related to the sensory organs. Eyes hold special status among all the sense organs because good vision is crucial for social and intellectual development of human beings. Hence authentic classics prescribed several preventive and curative measures for the management of ophthalmic disorders. Among them, topical treatments are very unique, effective in the management of eye diseases and are called "*Netra Kriyakalpa*". *Netra Kriyakalpa* have very fast action on the target tissues of eye. *Anjana* is a medicinal preparation which is applied on the lower palpebral conjunctiva or the cul-de-sac. Its active principles may be transferred to the interior of the eye according to their hydrophilicity and lipophilicity mainly through the conjunctiva and cornea by paracellular and transcelullar pathways respectively. pH, viscosity, tonicity, molecular size and molecular weight of the active ingredients are highly responsible for the absorption of Anjana. According to its form *Anjana* is of 3 types i.e. *Gutika*, *Rasakriya* and *Churna*. *Gutika* and *Churna* types of *Anjana* can be correlated with ophthalmic suspensions and *Rasakriya* type is with aqueous solutions/eye drops. *Gutika* and *Curna Anjana* have micro particles which may be deposited in the cul-de-sas and thereby increase the bioavailability to enhance ocular absorption. *Anjana* therapy may be highly beneficial in the anterior segment disorders because of the presence of several anatomical, biological and physiological ocular barriers. However it gives better results on the posterior segment disorders also.

KEYWORDS: *Anjana, Netra Kriyakalpa*, Hydrophilic, Lipophilic.

INTRODUCTION

Shalakya Tantra is one of the eight specialties of *Ashtanga Ayurveda* which deals with diseases which occur above the clavicle specially the sensory organs i.e. Eyes, Nose, Ears and Tongue. Eyes hold special status among all the sense organs because good vision is crucial for social and intellectual development of human beings and the knowledge from direct observation (*Pratyaksha pramana*) can be achieved only by eyes. Other sense organs also depend on the eye sight for their accuracy as quoted by ancient sage Vagbhata.[1] He said that for a man without eyes this world is useless because day and night are same for them even if the other sensory organs are healthy. Thus Vagbhata recommended that all efforts should be performed to protect the eyes throughout the life. Hence authentic classics prescribed several preventive and curative measures to protect the eyes. Almost all the *Acharyas* prescribed several treatment procedures for the management of ophthalmic disorders such as systemic, surgical, para-surgical and local or topical treatments. Among these several types of treatment modalities local treatments are very specific, effective and unique to the eye diseases and called as "*Netra Kriyakalpa*". It is similar as *Panchakarma* in *Kayachikithsa*. *Netra Kriyakalpa* have very fast action to the target tissues including posterior segment of the eye.

There are seven *Netra Kriyakalpas namely Akshi Tarpana, Putapaka, Seka, Aschyotana, Anjana, Bidalaka* and *Pindi*. The first 5 procedures were mentioned in *Susruta Samhitha*[2] and last two were prescribed only in *Sharangadhara Samhitha*[3] along with other 5 procedures.

- *Akshi tarpana* – Give nourishment to eyes through oily preparations.
- *Putapaka* – Same as *Akshi Tarpana* but drug should be prepared according to *Putapaka* preparation method.
- *Seka* – Pour liquid medicinal preparations into closed eyes and more beneficial for acute conditions.
- *Aschyotana* – Same as *Seka* but *Aschyotana* is poured into open eyes and it is the foremost procedure for all the eye diseases.
- *Anjana* – Indicated as curative and preventive measure. It should be applied only in *Dosha Pakva Avasta*.
- *Bidalaka* – Medicated paste is applied around the eyes except the eyelids in early stage of eye diseases. It is helpful as it increases the blood circulation to the eyes.
- *Pindi* – Same as *Bidalaka* but medicinal paste is kept over whole eye including lashes.

Allopathic system of medicine also developed several ocular treatment modalities and can be divided into four main divisions as systemic administrations, periocular injections, intraocular injections and topical instillations. Topical instillations included eye drops, eye ointments, gels, ocuserts and soft contact lenses. These topical instillations can be correlated with *Kriya Kalpas*.

- Eye drops – May be in the form of aqueous solutions or aqueous suspensions. It gives quick action and diluted immediately by tears.

- Eye ointments – Increases the bioavailability of the drug by increasing tissue contact time and by preventing dilution and quick absorption but cause blurred vision.
- Gels – Have prolonged contact time and do not cause much blurred vision.
- Suspensions - Dispersion of finely divided insoluble active pharmaceutical ingredients in an aqueous solvent consisting of a suitable suspending and dispersing agent which increases the bioavailability.
- Ocuserts – Can be placed in the upper or lower fornix up to a week and allow drug to be released at a relatively constant rate.
- Soft contact lenses – Very good for delivering higher concentrations of drugs in emergency treatment.

Among all these *Kriyakalpas Anjana* has unique therapeutic efficacy for several types of ophthalmic disorders and highly recommended as preventive measure of eye diseases in the *Ayurvedic* system of medicine. A number of ancient *Acharyas* prescribed *Anjana* therapy as daily regimen especially Sauvira Anjana (Animony sulphide) and *Rasanjana* (decoction of *Berberista aristata* – *Daruharidra*) mixed with bee honey as it eliminates *Kapha Dosha* from the eye because eyes have predominance of *Pitta Dosha* or *Teja Mahabhoota* for its proper functioning or clarity of vision.[4-6]

Apart from the *Ayurveda* the practice of *Anjana* was prevalent during Indu valley civilization for prevention of diseases as well as cosmetic purposes. *Anjana* is also mentioned in *Atharvaveda* however a detailed description is found in Sushrutha Samhita, Ashtanga Hridaya, Ashtanga Sangraha and Sharangadhara Samhita which are described its classification, form, dosage, method of application, indications and contraindications etc. "*Anakthi thi Anjanam*" is the definition of *Anjana* and word root is Anji because it gives moving, cleaning and clarity to eyes. [7] In this procedure a *Lepa* (semisolid or solid) is applied on the inner part of the lower eye lid from inner canthus (*Kaneenika Sandhi*) to outer canthus (*Apanga Sandhi*) with *Anjana Shalaka*.

AIMS AND OBJECTIVES

1. To review *Anjana* therapy according to the Ayurvedic point of view.
2. To study the probable mode of action of *Anjana* according to modern point of view.

TYPES OF *ANJANA*[8,9,10,11]

According to its form *Anjana* it is of 3 types i.e. *Gutika* (Pills), *Rasakriya* (Semisolid) and *Churna* (powder). Acharya Susruta and Vagbhata mentioned that the strength of *Anjana* increases in preceding order as *Gutika, Rasakriya* and *Churna*. However Acharya Bhavamishra mentioned that order somewhat differently as *Rasakriya, Varti* and *Churna*. Hence can be used *Anjana* according to the severity of the disease as *Gutika, Rasakriya* and *Churna* for the most severe, moderate and mild disorders respectively.

As per the action it is again three types namely *Lekhana* (sraping), *Ropana* (healing) and *Prasadana* (purifying). In Sharangadhara Samhita *Snehana* (oleation) and in Ashtanga Hridaya *Drishti Prasadana* (improve vision) type is mentioned instead of *Prasadana Anjana* in Susruta samhita.

Table 1: Composition of *Anjana*

Type of *Anjana*	Composition	Action
Lekhana	*Tikta, Kashaya, Amla, Katu, Lavana Tastes Kshara, Tikshna Guna*	Drain out *Doshas* from eye lids, vessels, sacs, *Srotas* & *Sringataka Marma* through mouth, nostrils & eyes
Ropana	*Kashaya, Tikta* + ghee/oil	Healing, improves the colour and visual acuity
Prasadana/Snehana/ Drishti Prasadana	*Madhura* + ghee/oil	Pacifying the *Doshas* in vision, oleation

INDICATIONS OF *ANJANA*

Anjana should be performed when symptoms of *doshas* are manifested and located only in the eyes and after the purification of body. Body should be purified by *Panchakarma* procedures i.e. *Nasya, Virechana, Vasti, Raktamokshana*.

Table 2: Indications of *Anjana*

Indication	*Susruta samhita*[12]	*Ashtangahridaya*[13]	*Sharangadhara Samhita*[14]	*Bhavaprakasha*[15]
After the *Dosha* manifested	+			
Dosha located only in eye	+	+		
After body purification	+	+		
Dosha become *Pakva*		+	+	+
Slight oedema in eye		+		
Severe itching in eye		+		
Sliminess of eye		+		
In thick eye secretions		+		
Vataja, *Pittaja*, *Kaphaja* & *Raktaja* disorders		+		

In addition to above indications Sharangadhara samhita[14] and Bhavaprakasha[16] recommended that the time of *Anjana* procedure according to the seasons.

In afternoon – *Hemanta* and *Sisira* In morning – *Grishma* In evening – *Sarath* Any time – *Vasanta* In rainy season *Anjana* should not be too much of cold or too much of hot.

Not only the seasonal recommendations; ancient *Acharyas* mentioned the time of *Anjana* application within the day also. Almost all of them recommended *Anjana* therapy only in the morning, evening and night neither in day time.[5,17] Preferably in the morning *Lekana* type of *Anjana* for *Kaphaja* diseases, in evening *Snehana* type for *Vataja* diseases and in the night *Prasadana* type for *Pittaja* diseases.[18]

Contraindications for *Anjana*[19,20,21]

Anjana process is contraindicated in those suffering from fatigue, *Udavarta*, excessive lacrimation, alcoholic, anger, fear, fever (especially early stage of fever), suppression of natural urges and disorders of head as it causes redness-discomfort-diminish of vision-discharge-pain in eyes. Also it should not be applied during the period of less sleep (causes incapability in function), in windy days (damage the visual acuity), on exposure to dust and smoke (causes redness of eyes), in the presence of eye discharge and *Adhimantha*-defective vision with pain (produces congestion and pain), just after the *Nasya, Vamana* and *Virechana* procedures (produces congestion and pain), in headache (causes disorders in the head), after a head bath, in excessive cold days and before sunrise (due to firmness of *Doshas)*, during indigestion (obstructs the channels-*Srotas*) and beginning of impulse of *Dosha*. Especially these contraindications are recommended for *Lekhana Anjana*.

Apart from above contraindications *Acharya* Bhavamishra advised that it should not be performed in excessively cold-hot-breezy days. If performed it will causes thickness, redness blindness due to a aggravation of respected *Doshas* and disturbs the sound sleep.[15]

Dosage of *Anjana*

Table 3: *Anjana* Dosage as Per the Susruta Samhitha[22]

Type of *Anjana*	*Lekhana*	*Prasadhana*	*Ropana*
Gutika	1 *Harenu*	1 1/2 *Harenu*	2 *Harenu*
Raskriya	1 *Harenu*	1 1/2 *Harenu*	2 *Harenu*
Churna	2 *Shalaka*	3 *Shalaka*	4 *Shalaka*

Note – *Hareṇu* is a Sanskrit technical word translating to "black cardamom". It is also known by the name *Hareṇuka*. The botanical name is *Vitex agnus-castu*, and is commonly known in English as "vitex", "chaste tree", "chasteberry".[23]

As per the Sharangadhara Samhitha[24],

***Gutikanjana* –** According to the potency of raw materials

Tikshna (high in potency) - 1 *Harenu*

Madhyama (moderate in potency) - 1 1/2 *Harenu*

Mrudu (mild in potency)- 2 *Harenu*

***Rasakriyanjana* –** According to the quantity of drug

Uttama matra - 3 *Vidanga*

Madhyama *matra* - 2 *Vidanga*

Heena matra - 1 *Vidanga*

Note: The meaning of *Vidanga* is a seed of *Embelia ribes* which is also known as false black pepper.

***Churnanjana* –** According to the action of drug

Virechana Karma - 2 *Shalakas*

Mrudu Karma - 3 *Shalakas*

Snehana Karma - 4 *Shalakas*

How to Perform *Anjana* Therapy[25,26]

Almost all the *Acharyas* prescribed it should be applied from the inner canthus to the outer canthus and vice-versa on the inner part of the eye lid or on the palpebral conjunctiva by using an *Anjana Shalaka* or physician's finger. But here they have not mentioned the exact eye lid ie. upper or lower. Hence it can be taken as lower palpebral conjunctiva or cul-de-sac because it provided enough space to application and easy to perform. Susruta and Vagbhata described the procedure in detailed. Physician should be hold the two eye lids separately with his left hand (with the thumb and index finger) and hold the *Anjana Shalaka* by his right hand. It can be applied several times which provides proper application and increases the bio availability. But it should not be applied excessively or with painful manipulation. Patient is asked to move the eyeballs upwards and rotate slowly which allows the medicine to spread over the eye. Also eyelids be moved slightly by eye massaging this might be helpful for increase absorption by enhancing blood circulation around the eyes. But blinking, squeezing or washing of the lids should not be done till the properly performed *Anjana* features appeared.

Eye wash with water or suitable medicines for the respective disease, *Doshas* or season is recommended as *Paschat Karma*. Otherwise remaining medicines may vitiate the *Doshas* and give rise to the disease and caused itching sensation. To control these *Dhumpana* (medicinal smoking) can be performed. *Pratyanjana* (restorative collyrium) can be applied to control the irritation as well.

However *Anjana* which are used as therapeutics should not be very strong or very weak in potency, very little or very large in quantity, too thin or too thick in consistency, very rough and too hot.[27]

***Samyakyoga, Atiyoga* and *Heenayoga* Features of *Anjana*[28]**

Acharya Susrutha explained well about the *Samyakyoga*, *Atiyoga* and *Heenayoga* features of *Lekhana, Prasadana* and *Ropana* types of *Anjana*. Features of properly performed *Anjana* therapy are known as *Samyakyoga Lakshana* whereas excessively performed features are known as *Atiyoga Lakshana*. Inadequately performed features are called *Heenayoga Lakshana*.

- *Samyakyoga Lakshana* of *Lekhana Anjana* are non sliminess of eyes, lightness of eyes, non discharging, swift in action, cleanliness of eyes and subsided the complications.
- *Atiyoga Lakshana* of *Lekhana Anjana* are deviation of eyes, hardness of eyes, discolouration of eyes, drooping of eyes, roughness of eyes and excessive discharge. All of the above characteristics features cause *Vata Dosha* vitiation which must be managed

Santarpana Karma (Saturation) along with other *Vata* alleviating measures.

- In inadequately performed *Lekhana Anjana Doshas* get more aggravated. This should be corrected by performing *Dhumpana* (medicinal smoking), *Nasya* (Snuffing) and *Anjana* therapy.
- In properly performed *Prasadana Anjana* eyes attain unctuousness-proper colour and strength, cheerfulness of eyes, cleanliness of eyes and it functions perfectly.
- If *Prasadana Anjana* is applied excessively, eye is affected with some mild disorders. In this case rough drugs should be used to pacifying *Dosha*.
- *Prasadana Anjana* applied deficiently becomes useless.
- All the features such as *Samyakyoga, Atiyoga* and *Heenayoga* of *Ropana Anjana* are same as *Prasadana Anjana* but results moderately.

Hence for the better efficacy proper dose of *Anjana* must be advised.

Materials Used in *Anjana Karma*

- *Anjana shalaka*
- *Anjana patra*
- Drugs are the essential materials for *Anjana Karma*.

Anjana Shalaka[29,30,31]

Anjana Shalaka or collyrium probe is a cylindrical rod with 8 *Angulas* in length which is made of metals, stones or horns of animals and ends should be bluntly pointed like a flower bud.

Anjana Patra[32]

The container used for the storage of *Anjana* is known as *Anjana Patra*. The material should be taken according to the medicinal property of the drug. It is further advised the *Anjana Shalaka* also can be made accordingly.

Routes of Ocular Drug Administration and Drug Absorption in Relation to *Anjana*

Drugs can be administered to eye by various routs such as topical, periocular, intraocular and systemic. Periocular route includes subconjunctival, sub-Tenon's, peribulbar and retrobulbar whereas intraocular route is consists of intracameral and intravitreal types. Among all these routes topical route is the most flavored route specially for the anterior segment and ocular surface disorders. However the route should be selected according to the target ocular tissue.

Anjana is a medicinal preparation which applies on the lower palpebral conjunctiva or the cul-de-sac. Therefore this can be taken as topical type of ocular drug administration. The major tasks of developing topical ocular drugs are increase the bioavailability and control or constant release of drug delivery. Because precorneal factors, anatomical barriers and systemic absorption are negatively affect the bioavailability.

Mainly affected precorneal factors include solution drainage, blinking, tear film, tear turn over and induced lacrimation.[33] Tear film offers the first resistance due to its high turnover rate. Lacrimal turnover rate is about 1 µl /min. Thus excess volume is flown to the nasolacrimal duct within a few minutes.[34] Mucin present in the tear film plays a protective role by forming a hydrophilic layer that moves over the glycocalyx of the ocular surface and clears debris and pathogens including ocular drugs also.[35] Human tear volume is estimated to be 7 µl. The cul-de-sac can transiently contain around 30 µl of the administered eye drop. However, tear film displays a rapid restoration time of 2–3 min, and most of the topically administered solutions are washed out within just 15–30 s after its instillation.[35] Blinking of eyes promote the drainage of instilled ocular drugs through the nasolacrimal duct. Each blinking removes about 2 µl of fluid from the cul-de-sac.[36] Due to the spontaneous tear flow instilled drugs are completely lost from the cul-de-sac in about 5 minutes and 80% of the drug lost through the nasolacrimal drainage.[37] Considering all the precorneal factors, contact time with the absorptive membranes is lower, which is considered to be the primary reason for less than 5% of the applied dose reaching the intraocular tissues.[36]

Eye is an extremely accessible organ foreign material. When considering anatomical barriers cornea and conjunctiva act as main barriers which are the most superficial layers of the eye. Cornea has five layers among them main three layers responsible for the drug transportation namely; outer lipophilic epithelium and Bowmen's membrane (which acts as a barrier for hydrophilics), middle hydrophilic stroma (which acts as barrier for lipophilics) and inner less lipophilic endothelium (which forms barrier to hydrophilics).[37] The tight junctions in the most superficial layer of corneal epithelium limit the paracellular drug permeation.[38] It serve as selective barrier for the small molecules and completely prevent the diffusion of large molecules.[37] However lipophilic drugs have higher permeability than hydrophilic drugs via the corneal epithelium.[39] Despite the high permeability of liphophilic drugs corneal pores in between the tight junctions allow to penetrate small hydrophilic molecules (<3nm).[37] Corneal stroma is hydrophilic in nature and a relatively open structure. Molecular weight up to 500,000 kd and hydrophilics can pass through it and it is comparatively act as a barrier for lipophilics.[37] Endothelium offers little resistance for the drugs due to the presence of gap junctions. Due to biphasic solubility nature of cornea both the liphophilic and hydrophilic molecules can pass through it. Especially liphophilics travels through the transcellular pathway and hydrophilic molecules from the paracellular pathway (through the tight junctions of epithelium) both by diffusion.[37] Thus the transcorneal permeation is the main route of drug entrance from lacrimal fluid to the aqueous humour. From the aqueous homour drugs can easily enter to the ciliary body and iris where the drug may bind to the melanin. This forms a reservoir which is released drugs gradually to the surrounding cells which prolonging the drug activity.[40]

The superficial layer of the conjunctival epithelium has tight junctions which are act as the main barrier for the drug penetration. In here also lipophilic drugs can diffuse through transcellular pathway and hydrophilic drugs passage through the paracellular

pathway.[37] The conjunctiva is more permeable than the cornea and its surface area is 20 times greater than that of cornea. Thus its permeability to hydrophilic drugs is higher than that of cornea and molecular weight 20,000-40,000 kd can pass through the conjunctiva.[41,42,43] Conjunctiva is a highly vascularised structure; hence it is a major route for systemic drug absorption after topical instillation.[44] This systemic absorption reduces the bioavailability and drug transportation to the target ocular tissue. Not only the cornea and conjunctiva; sclera also plays an important role on the drug absorption. However it is more permeable to lager molecules than conjunctiva and cornea.[45] It is poorly vascularized and consists mainly collagen and mucopolysaccharides through which drugs can diffuse to the vitreus.

Another way of bioavailability reduction is systemic absorption. Drugs can reach the systemic circulation after topical ocular delivery by several routes such as through the aqueous humor, ciliary body, iris, eyelid margins and especially via the nasal mucosa. Systemic absorbed drugs have to cross the blood ocular barriers to reach the target ocular tissue and have less chance of reaching ocular tissues. Regarding *Anjana* therapy considerable amount of drug may pass to the nasolacrimal duct due to increased lacrimation and then undergo to systemic absorption. In addition to nasolacrimal drainage by tear evaporation, drug binding to proteins in tear, drug metabolism by tear enzymes also responsible for reduce the drug absorption amount.

Anjana therapy as a kind of topical administration may be highly activated in the anterior segment of the eye which is up to the crystalline lens. Its active principles may be transfer to the interior of the eye according to their hydrophilicity and lipophilicity mainly through the conjunctiva and cornea respectively.

PHARMACOKINETICS OF *ANJANA*

The process of drug uptake by the body, distribution to the target tissues, its biotransformation or its metabolism and the method of excretion from the body is known as pharmacokinetics of a drug. The main drug absorptions methods to eye is consists of passive diffusion, carrier mediated transport (facilitated diffusion and active transport) and endocytosis.[37] Passive diffusion refers to the process of movement of drug molecules across the biological barrier accordion to its concentration. It does not need energy and this is the primary mode of drug transport across the ocular surface. Passive diffusion also depends upon the degree of ionization (pH) and lipid solubility of the drug.[37] Also some drugs are transported cross the biological barriers by carrier mediate transport. In this method carrier molecules presented on the membrane surface forms a complex with the drug molecule. Carrier mediated diffusion of molecules along the concentration gradient is known as facilitated diffusion which does not require energy. Its rate of diffusion depends upon the ability of drug molecules to bind with the carrier and the availability of carriers.[37] Active transport refers to carrier mediated drug transport against the concentration gradient; it requires energy. Uptake of drug molecules by plasma membrane derived vesicles is named as endocytosis. Therefore all the topical instillations including *Anjana* transport cross the conjunctiva, cornea, sclera, iris, ciliary body, lens ect via the above mentioned drug absorption methods.

According to its form *Anjana* is 3 types i.e. *Gutika, Rasakriya* and *Churna*. Hence the *Gutika* and *Churna* types of *Anjana* can be correlated with ophthalmic suspensions and *Rasakriya* type is with aqueous solutions/eye drops. *Rasakriya Anjana* is completely soluble without any sedimentation hence it can be compared with modern eye drops. Because of its solubility and micro molecules it can be rapidly and easily absorbed but its drainage out from the cul-de-sac is rapid. Thus its bioavailability and rate of ocular absorption is comparatively lesser than the other two types of *Anjana* forms. *Gutika* and *Churna* types of *Anjana* have sedimentated micro particle; so that these types can be correlated with ophthalmic suspensions. Suspensions are non-invasive ocular topical drop drug carrier systems which can be defined as dispersion of finely divided insoluble active pharmacological ingredients in an aqueous solvent consisting of a suitable suspending and dispersing agent. Suspension particles retain in cul-de-sac and thereby improve drug contact time and duration of action relative to drug solution. Duration of drug action for suspension depends upon the particle size of the drug.[46] Because suspensions contain micronized drug molecules most preferably less than 10 µm in diameter.[37] Therefore particle size of active agent plays a key role because sedimentation rate, agglomeration and resuspendability are totally affected by the size of particles. Suspensions' drug delivery system takes place in two phases i.e. rapid and slow. Small particle size promotes fast dissolution and fast absorption but these small particles tend to easily drain out from the cul-de-sac which may results decrease the bioavailability and absorption. Mean while lager particle size helps retain particles for longer time and slow drug dissolution.[37] Thus an optimal particle size is expected to result in optimum drug activity.

In case of *Anjana* preparation *Gutica* and *Churna* types prepared by dry milling, grinding and micro pulverization which are the processes help in getting optimal particle size but still it has not standardized the best particle size. Thus it can be taken as <10 µm because that size generally minimizes the ocular irritation. As per the modern pharmacology ophthalmic suspensions should be formulate according to the following steps with proper sterilization method.[47]

1. Preparation of a dispersion of the drug
2. Preparation of the structured vehicle, followed by addition of the drug dispersion
3. Addition of the other adjuncts – preservatives, wetting agents, suspending agents ect.
4. Homogenization

All the above 4 steps are followed by *Anjana* process except the adding specific preservatives because drugs itself act as preservatives and most of the time freshly prepared drugs are use in Ayurveda. Meanwhile bee honey, ghee, breast milk and some of the medicinal fresh juices commonly use as vehicles and wetting agents. Hence it should be carefully monitored for the proper maintenance of sterilization of the drug. Moreover

optimum pH, tonisity and viscosity of the preparation are play a significant role on its bioavailability and amount and rate of absorption.

PROBABLE MODE OF ACTION OF *ANJANA*

Once applied an *Anjana* it acts as a foreign body to ocular surface. Hence eye gets reflex secretion in response to foreign particles on cornea and conjunctiva. Due to that considerable amount of drug washes out from the eye by weeping and another major portion may drainage to the nasolacrimal duct (NLD). Apart from these another part may be eliminated from the ocular surface by evaporation (mainly *Rasakriya Anjana*), metabolization by tear enzymes and get in contact with tear proteins. Finally it mains in the cul-de-sac a very less amount of *Anjana* for the ocular absorption; meanwhile the portion drainage to the NLD may absorb to the systemic circulation by nasal-laryngeal and oral mucosa. On the other hand *Gutika* and *Churna Anjana* have micro particles which may be deposited in the cul-de-sac and thereby increase the bioavailability to enhance ocular absorption.

The ocular absorption of *Anjana* may initiate though the conjunctiva and cornea. Mainly lipophilic active ingredients may absorb through the cornea by transcellular pathway and hyrophilics from the conjunctiva by paracellular pathway. This ocular absorption may be depend on the passive diffusion, carrier mediated transport (facilitated diffusion and active transport) and endocytosis. Also pH, viscosity, tonicity and most importantly molecular size and molecular weight of the active ingredients play a major role of the same. Once it crosses the conjunctiva (mainly hydrophilics); the sclera is more permeable and it allows drugs to penetrate the other interior structures of the eye i.e. ciliary body, iris, aqueous houmer, lens, vitreous ect. But due to high vascularization of conjunctiva, ciliary body and iris considerable amount of drug may be enter to the systemic circulation again. The drugs pass though the corneal epithelium (mainly lipophilics) directly goes to the aqueous humour and distribute to the other ocular tissues. However some of the drugs coming to the aqueous humour either via cornea or conjunctiva are undergo to metabolization by the enzymes present in the aqueous.

Considering all these factors it can be said that *Anjana* therapy may be highly activated in the anterior segment of the eye because of the presence of several anatomical, biological and physiological ocular barriers. But in the system of Ayurveda pharmacological actions of a drug may explain according to its pharmacological properties which are included *Rasa, Guna, Virya, Vipaka* and *Prabhava*. These qualitative qualities are still not explained and interpritated in accordance to the modern science. Hence as per the view of Ayurveda these qualitative measures may act on the posterior segment of the eye.

DISCUSSION AND CONCLUSSION

Considering all of above discussed factors *Anjana* therapy is a holistic, well developed method of topical ocular drug administration which is described in detail with its indications, contraindications, application method, pre and post procedure measures, dosage forms and even proper storage advices in authentic texts. It can be taken as a further development of *Ashyotana* due to its increased bioavailability on the ocular surface than the *Ashyotana*. Not only that ancient *Achryas* advised some processes to overcome some practical difficulties of *Anjana* therapy too such as *Anjana* should be applied from medial canthus to lateral canthus and vice- versa; which increases bioavailability, just after the application the patient is asked to move the eyeballs upwards and rotate slowly which allows the medicine to spread over the eye, eyelids should be moved slightly by eye massaging with close eyes this might be helpful for increase absorption by limiting nasolcrimal drainage. However the exact mode of action of the *Anjana* therapy is still not proved by any experimental studies. Hence now it is high time to prove our ancient knowledge in accordance to modern point of view.

High ocular irritation and less contact time are the main problems in *Anjana* therapy. Ocular irritation can be minimize by using the optimal particle size (<10 µm) and using pH between 6.5 to 7.6; which is the pH value of normal tears. Meanwhile bioavailability can be increase by using optimal viscosity and tonicity. The optimal viscosity for ophthalmic preparation is 12-15cp and optima tonicity is 266-445mOsm/kg. Normally instilled drugs completely disappear from the cul-de-sac in about 5 min specially eye drops. Thus if the second drop is applied 5 min after the 1st drop then no washout effect occurs on the 1st drop. Hence this theory can be applied for the *Rasakriya Anjana* for optimal results; however for the *Churna Anjana* and *Gutika Anjana* have higher bioavailability itself.

Most of the modern topical ocular preparations are not able to reach up to the posterior segment. But *Anjana* is a good, simple, easy and effective treatment modality for treating both the anterior and posterior segment disorders of the eye which is being practiced more than 5000 years. Finally it can be concluded that *Anjana* is an ideal remedy for various types of ophthalmic disorders; which can be used as preventive as well as curative measure.

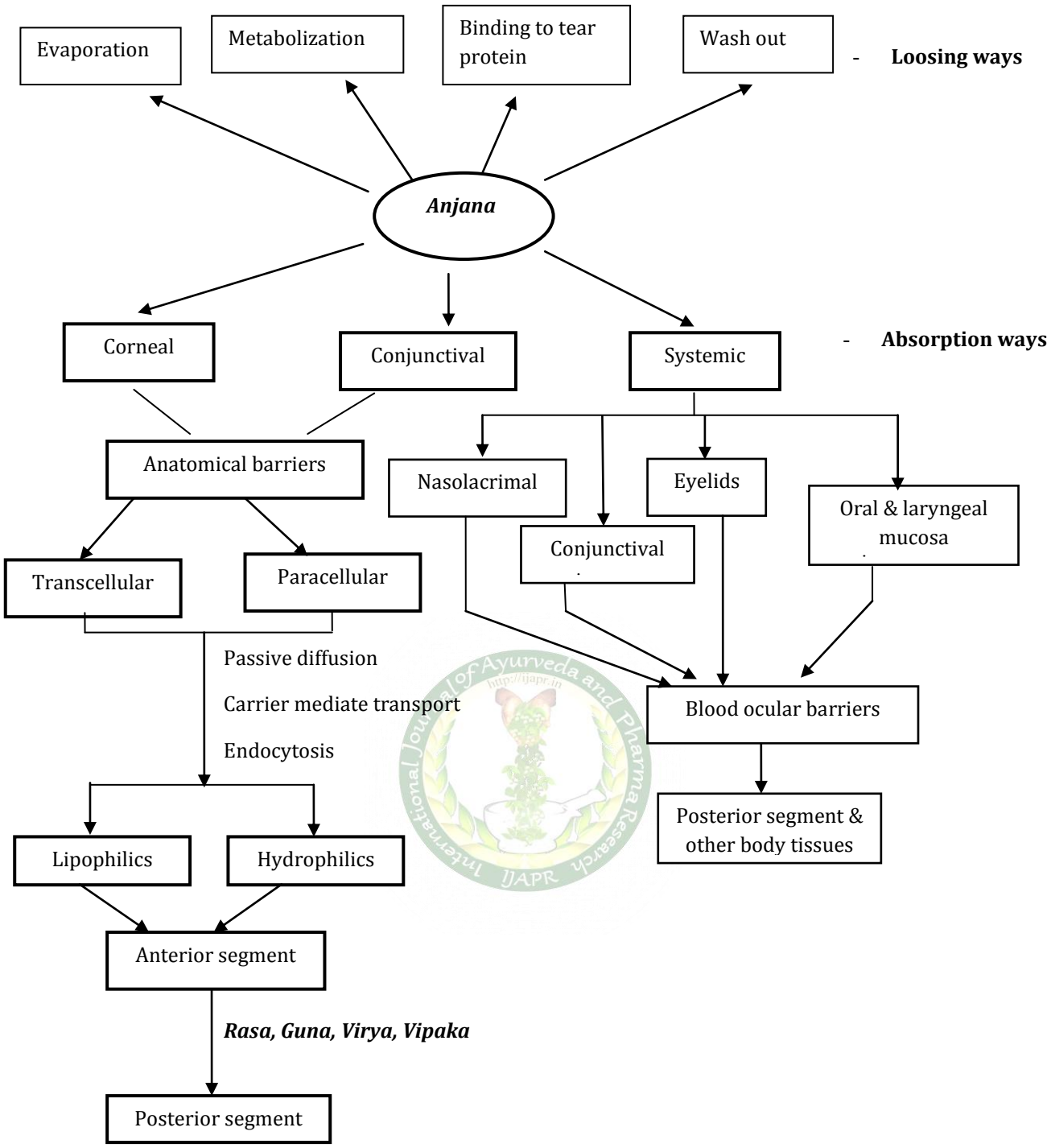

Figure 1: Schematic diagram of probable mode of action of *Anjana* therapy

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***Address for correspondence**
Dr Kankanan Gamage Surangi
MS Scholar,
Department of Shalakya Tantra,
National Institute of Ayurveda,
Jaipur, Rajasthan, India.
Ph: 07665539668
Email: surangikg@gmail.com