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REVIEW ARTICLE OPEN ACCESS

AN INSIGHT INTO *SNEHA KALPANA* VIS-À-VIS LIPOSOME

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ABSTRACT:

The lipid-based formulation known as *Sneha Kalpana* contains both *ghrta* and *taila. Sneha kalpana* is a pharmaceutical process used to prepare oleaginous medications from substances like *kalka, kwatha* or *dravya dravya* taken in a specific ratio and heated for a specific amount of time. *Sneha kalpana* can be compared with Liposomal system of drug delivery. The present study highlights the importance and superiority of lipid-based preparations from modern and *Ayurvedic* perspectives. The lipids are used externally and internally in *Ayurveda.* It has the potential to bypass the blood-brain barrier. The liposomal mechanism of drug delivery is an advancement in the modern medical system. Simple microscopic vesicles are called liposomes which completely surround an aqueous volume in a lipid-based membrane. In this review, we summarize the main applications of liposomes, the superiority of *Sneha kalpana* and the comparison of *sneha kalpana* with liposomes.

Keywords: *Sneha kalpana,* Liposomes, Bio availability.

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INTRODUCTION

Ayurveda has a unique dosage form known *as Sneha kalpana*. The main objective of this *kalpana* is to deliver the active lipid-soluble and aqueous ingredients into the *sneha. Sneha* is used in all modes of drug administration procedures including *Pana, Abhyanga, Bhojhana, Nasya, and Basti*. Nowadays in the field of pharmaceutics, new dosage forms are continuously emerging with the primary goal of increasing the drug's bioavailability which in turn shows a maximum therapeutic response. Liposome is an example of an advanced dosage form in which nanoparticles comprising lipid bilayer membranes surrounding an aqueous interior are formed. For the liposomal drug delivery system, a considerable amount of effort has been put into formulating these medications in dosage forms for sustained and controlled release for oral and parenteral administration. *Sneha kalpana* and liposomes are two dosage forms that are quite similar in their origin and both of them have lipoidal structures as their base.[1]

SNEHA KALPANA

One part of "*Kalka dravya*," four parts of "*Snehadravya*," and sixteen parts of "*drava dravya*" are combined to make "*Sneha Kalpana*." The mixture is boiled until '*Sneha - siddhi lakshana'* are attained.[2] *Taila* and *Ghrta* are important preparations in the *Ayurveda* pharmaceutics.

Sneha siddhi lakshana[3]

- *Sneha kalka* when rolled between thumb and index finger produces wick shape.
- There should not be any sound when *sneha kalka* is sprinkled over fire.
- Appearance of foam in *taila paka* and disappearance of foam in *ghrita paka*.
- Desired colour, odour and taste of the ingredient become marked when *sneha paka* is completed.

The main aim of *Sneha kalpana*[4]

- To extract lipid soluble active principle from the drugs.
- To utilize the medicinal properties of *taila/ghrta.*
- To enhance the drug absorption.
- To prolong shelf life of *sneha*.

LIPOSOMES

The word Liposome is derived from two Greek words: lipo means fat and soma means body. It has named as liposome because its composition is primarily of phospholipids. Liposomes are made of generally biocompatible and biodegradable materials and have an aqueous volume enclosed by one or more bilayers of natural and/or synthetic lipids. Liposomes are being

extensively researched as drug carriers to improve the delivery of therapeutic agents.[5]

MECHANISM

A liposome is made up of an aqueous solution core surrounded by a lipid bilayer membrane that is hydrophobic and prevents the passage of hydrophilic solutes dissolved in the core. Chemicals that are hydrophobic bond with the bilayer. A liposome may contain both hydrophobic and/or hydrophilic molecules. The lipid bilayer can combine with other bilayers, like the cell membrane, to transport the molecules to the site of action, but this is a complicated and unnatural process that does not apply to the delivery of nutrients and drugs.[6]

As a result, the use of liposomes for the controlled and targeted drug delivery in the treatment of viral infections, cancer and other microbial disorders has received extensive evaluation. Heating is not only the required method of preparation (as the case with products of *sneha paka*) while making liposomes; additional techniques like sonication, homogenization, shaking, etc. are also used. The water-soluble component stays in the aqueous region, whereas the lipid-soluble compound stays in the outer lipid bilayer. Considering the above facts, it is assumed that *sneha* prepared may have the same structure and function of liposomes or liposomes are a modified or developed form of the original *sneha kalpana/paka.*[1]

CLASSIFICATION

Based on the ability of liposomes to interact with the cells

Non - interactive sterically stabilized (long - circulating) liposomes (LCL).

Cationic liposomes with high interactivity.

Depending on the size and number of bilayers

Multilamellar vesicles (MLV)

Large unilamellar vesicles (LUV)

Small unilamellar vesicles (SUV)

Based on composition and mechanism of intracellular delivery

Conventional liposomes (CL)

Ph - sensitive liposomes

Cationic liposomes

Immuno liposomes

Long - circulating liposomes[5]

Advantages, Disadvantages and applications of Liposomes[5]

Advantages of Liposomes

- Biodegradable.
- Biologically inert.
- Produce no antigenicreaction.
- Minimum side effects and limited intrinsic toxicity.
- Biocompatible.
- Improved pharmacokinetic Properties.

Disadvantages of Liposomes

- Difficult to sterilize and manufacture on a large scale.
- Leakage of encapsulation during storage.
- Very high production cost.
- Physical/Chemical stability.
- They exhibit osmotic sensitivity.
- They are permeable to water.
- Cations cannot pass through positively charged membranes, while anions can pass
- through negatively charged membranes very easily.

Properties of liposomes[7]

The system is made up of bimolecular sheet structures intercalated with aqueous space.

Table 1: Liposomal medications with clinical approval[5]

Name	Indication
Liposomal amphotericin B	Fungal infections
Liposomal IRIV Vaccine	Hepatitis A, Influenza
Liposomal morphine	Postsurgical analgesia
Liposomal daunorubicin	HIV - related Kaposi's sarcoma
Liposomal cytarabine	Malignant lymphomatous meningitis
Liposomal Verteporfin	Pathologic myopia, Age - related macular degeneration, ocular histoplasmosis.
Liposomal doxorubicin	Cyclophosphamide-based combination treatment for metastatic breast cancer

Comparison of *Sneha Kalpana* and Liposome[1]

Table 2: Comparison between *Sneha kalpana* and Liposome[1]

Characteristics	*Sneha kalpana*	Liposome
Origin	Oleaginous	Oleaginous
Formation	Interaction between aqueous and oil	Interaction between lipid-Lipid and lipid water molecule
Structure	Not exactly known	Lipid bilayer
Method of	Heating, *Aditya paka*	Heating, Sonication, Homogenization,

preparation		Shaking
Mode of administration	*Pana, Abhyanga, Nasya, Vasti,Gandusha, Karna purana, Netra kalpa*	Oral, I.V., Topical

Origin of both *Sneha kalpana* and liposome is oleaginous, which means from *sneha*. *Sneha kalpana* is the unique formulations prepared by using either *taila, ghrta* or such other fatty substances as the base. *Sneha yoni* is *Sthavara* and *Jangama*. These are the two *yoni* or origin or sources of *sneha*.[8] Liposome is one such dosage form in which membranes are usually made of phospholipids. The word 'lipo' means fat, indicates the origin of liposomes and its relation with fat.[9] In *Sneha kalpana* there is an interaction between aqueous and oil. This interaction happens between the *sneha* and *drava dravya* mainly during the *sneha paka*. In case of liposomes an aqueous volume is entirely enclosed by a membranous lipid bilayer.[10] So the structure of liposome is lipid bilayer. But the structure of *sneha* is not exactly known. Method of preparation of *sneha kalpana* is by heating. Here the specified quantity of *kalka dravya*, *murchita ghrta* or *taila*, *drava dravya* are to be mixed together and boiled on *mandagni* till only *ghrta/taila* part remains.[2] *Aditya paka* method is another preparation of *sneha kalpana* using sun rays. In this method *kalka dravya* along with *sneha* are kept in sunlight for certain duration of time. Sometimes along with the *kalka dravya, drava dravya* may also be added. In this method the *sneha siddhi lakshana* are not mentioned, but few opines that colour of *patra* (vessel) should change after the proper *paka*. *Rasa dravya* and more volatile principles are commonly used in this method.[11] The method of preparation of liposomes is by heating,[12] sonication, shaking.[9] Heating is a main method of preparation for both *sneha kalpana* and liposomes. The mode of administration of each *sneha paka* is different. *Mridu paka* is for *nasya* (through nasal route. *Madhyama paka* is for all other purposes e.g., *pana*, *basti etc* (through oral, rectal route etc.). *Khara paka* is for *abhyanga* (External application/Topical route). *Ama/dagdha paka sneha* is not recommended for therapeutic use.[13] Likewise, the mode of administration of liposomes is through Oral, Topical routes,[14] I.V. [15] So *Sneha kalpana* has more similarities with liposomes, so it can be compared with the liposomes for their characteristics.

Application of Liposomes[16]

- Liposomes as drug delivery vehicle.
- Liposomes as vaccine carrier.
- Liposome in tumor therapy.
- Liposome in gene therapy.
- Liposomes as artificial blood surrogates.
- Liposomes as radio - pharmaceutical and radio - diagnostic carrier.
- Liposomes in cosmetics and dermatology.
- Liposomes in enzyme immobilization.

Liposome as a vehicle for drug delivery:

- Liposomes improve the solubility of medications (Amphotericibin-B, Cyclosporin, Paclitaxel, Minoxidil).
- Provide protection to sensitive drug molecules (DNA, RNA, Ribozymes, Cystone arabinose).
- Increasing intracellular uptake (anti-cancer, anti-viral & anti-microbial agents).
- Modify the pharmacokinetics and medication distribution.

Liposome as vaccine carrier:

- Liposomes enhance both humoral and cell-mediated immunity.
- Liposomal vaccines based on immunopotentiating reconstituted influenza virosome (IRIV) are prepared.
- Liposomes can incorporate immunomodulating substances like lipopolysaccharide, lipid, and muramyl dipeptide for the purpose of immunopotentiation.

Liposome in tumour therapy:

- Liposomes can be given intravenously as drug carriers.
- If liposomes are made more hydrophilic by adding lipids, their bloodstream circulation time increases.
- These are stealth liposomes, which are employed as delivery systems for hydrophilic anti-cancer medications (Doxorubicin, Mitoxantrone).
- They have the ability to extravasate the tumor's vascular endothelium in this state.

Liposome in gene delivery:

- The potential for gene delivery in non-viral vector systems, in particular modified liposomes such as cationic liposomes, fusogenic liposomes, genosomes, lipoplex, and

lipopolyplex, has been extensively investigated.

- Cationic liposomes transfer the content through membrane fusion, preventing DNA destruction in lysosomes and nuclei.
- Genosomes are complex combinations of cationic liposomes and DNA.

Liposomes as artificial blood surrogates:

- Products with liposome-encapsulated haemoglobin can be employed as artificial RBCs.
- Better oxygen carriers are sterically stabilised liposomes carrying haemoglobin.
- These are less toxic, cause less platelet aggravation and activation, and produce less hemostasis.

Liposome as radio - pharmaceutical & radio - diagnostic carrier:

- Imaging of the liver, spleen, brain, lymphatics, tumour, blood pool, cardiovascular diseases, visualisation of inflammation, infection sites, bone marrow, and eye vasculature are some of the Liposomal radio - diagnostic applications.
- Liposome imaging agents are used for computed tomography, magnetic resonanace, & ultra sound imaging of tumours.

Liposome in cosmetics and dermatology:

- Liposomes combined with essential oils offer a nourishing therapy that works well and penetrates the skin deeply.
- Liposomal preparation reduces roughness by interacting with corneocytes, which produces an intracellular lipid that softens and soothes the skin.
- There are several liposome-based products available for skin and body care, cosmetics including mascara and foundation, hair care, sunscreen and perfumes.

Enzyme immobilization

- Enzymes can be delivered by liposomes to the lysosomal system and other locations.
- β-glucosidase & α-glucosidase are loaded in liposomes for treatment of Gauchers & Pomps disease respectively.

DISCUSSION

Sneha is preferable to other administration methods for the following reasons:

In Gastro -intestinal tract:

The degree of ionisation, molecular weight, and lipid solubility of the medicine influence the absorbtion of a drug in to the gastro intestinal tracts. Lipid soluble drugs are normally absorbed easily.[17]

In topical routes:

Absorption of drugs given topically is influenced by Drug concentration, lipid solubility and local blood flow. Participants who underwent *sneha abhyanga* (body massage) showed significant changes in their brain's functional activation as well as an increase in cerebral blood flow. Stress-related hormones such as chromogranin A, arginine vasopressin, and serum cortisol were all decreased by massage.[18] A gentle oil massage may loosen the tight junctions that exist between endothelial cells and the CNS vessels, allowing solutes and other substances to enter the CNS more easily. Procedures like *shirodhara, shirobasti, shiroabhyanga* shows similar effects.[17]

In parenteral route:

Drug action is faster in this route. There are no chances of interference by food or digestive juices. Liver is bypassed.[19] The absorption from the site is influenced by the local vascularity of the regions. Oil-based preparations are slowly absorbed and aqueous formulations are absorbed quickly.[17] The rate of absorption is favoured by local warmth and massage. This is the underlying idea behind how various kinds of oil enema work, where the effectiveness and retention time are directly proportional to each other. e.g., *Matravasti*. Compared to *Kashaya vasthi, Matra vasthi* has more retention time and it will be more effective. *Basti dravya* have to retain in the body for enough time for getting desired action. If *basti dravya* returns much earlier, it cannot produce the desired *snehana* effect in the body.[20]

Superiority of Lipids in CNS disorders:

Entry of drugs into central nervous system is limited by blood brain barrier (BBB). It is a hypothetical barrier which exists between plasma and extracellular surface of brain. This barrier is constituted by glial cells and capillary endothelium in the brain. Only lipid - soluble, non - ionised drugs readily pass through this barrier.[21] Lipid solubility and a concentration gradient across the cell membrane are responsible for the easy entry. Intranasal administration of dry herbal powders or medicinal oils is known as *Nasya*. *Nasya* or nasal administration of drugs is specially indicated in all types of *Urdhwa jatrugata vikara.*[22] The mucous membrane of the nose can readily absorb many drugs, digestive juices and liver are bypassed.[19] It is a practical, non-invasive, quick and easy way to deliver the

therapeutic chemicals into the CNS. Rapid delivery, bypassing the BBB and direct CNS targeting minimise systemic exposure and adverse effects. The use of medicinal ghee is important in the *Ayurvedic* treatment of neurological and psychiatric disease like *Unmada, Apasmara, Vatavyadhi, etc.* Ghee is considered as the best among all the varieties of *Sneha*. It is cooling and provides lengthy span of life.[23] But research studies on this subject are lacking.

In Transplacental transfer:

Entry of drugs into foetal circulation is restricted by blood placental barrier (BPB). It is also a hypothetical barrier which exists between maternal and foetal circulation. It permits the entry of only lipid - soluble and non - ionised forms of drugs.[21] When describing *Garbhiniparicharya* (prenatal care), the necessity of preparation and vehicle in the form of fatty medium, such as *ghrita, navaneetha, ksheera* etc are mentioned. In the *masanumasika pathya ahara* of *garbhini* the use of medicated milk, *ghrita, garbhasthapaka dravya,* etc. are mentioned.[24]

CONCLUSION

Sneha kalpana is widely used both internally and externally. It is an effective and potent *kalpana.* Lipid based drug delivery system enhances the shelf life, bio-availability, absorbability and safety. It can be utilized to transport medications to deeper tissues within the blood - brain barrier and the placenta, facilitating the entry of formulations' active ingredients into the brain and foetus. Liposomes have an important position in modern technology. The study of liposomes will become a more sophisticated and dependable platform for the creation of more beneficial bioproducts, particularly in the fields of public health and medical diagnostics, as other medical technologies evolve.

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