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MODIFICATION OF SNEHA KALPANA AS A NOVEL DOSAGE FORM –PHYTOSOMES

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ABSTRACT

Pharmaceutics is the branch of science dealing with process of converting old drugs into medicationthat can be used as medicines effectively by patients. Ayurvedic Pharmaceutics (*Rasa shastra* & *Bhaishajya Kalpana*) offers many judicious processing techniques (*samskara*) to convert/modify these substances into different physical forms (dosage forms) without compromising the palatability, safety and efficacy. Ayurvedic Pharmaceutics is also called as Bhaishajya Kalpana. The basic classical formulations of Bhaishajya termed as Panchvidha Kashaya other than these are *Sneha Kalpana*, *Sandhan Kalpana*, *kshar Kalpana*, etc, Novel Drug Delivery systems is combination of the advance techniques and the new dosage forms. Some herbal Phyto molecules are poorly miscible with oils and other lipids and often fail to pass through the small intestine because of its lipoidal nature. The effectiveness of any herbal product is dependent upon delivering an effective level of the active compounds. The phytosome as NDDS meets this challenge by markedly enhancing the bioavailabilityof selected phytomedicine. *Sneha Kalpana* can be administered as Phytosomes is reviewed in this article using classical texts and various literature available in various journals. This review helps to demonstrate advancement of *Sneha Kalpana* as Phytosomes.

KEYWORDS: Sneha Kalpna, Phytosomes, Phospholipid.

INTRODUCTION

Ayurveda is the scientific entity dealing in therapeutic and holistic way of treatment, and uses medicinal plant as main source of therapeutic treatment in various diseases. Medicinal plants are presently in demand and their acceptance is increasing progressively. The term medicinal plant refersto a variety of plants that have medicinal properties. These plants are a rich source of compounds that can be used to develop drug synthesis.[1] Substances distributed in the universe are derived fromplants, animals or minerals, which also serve as the drug sources and hence are considered as basic drug classes. *Charaka Acharya* said Drugs usually are known to possess destructive potential and hence need to be used carefully. He further elaborates the concept by saying that not a single substance in the Universe is devoid of therapeutic potential and hence is a potential drug source, provided it is used judiciously at appropriate indications. Plant, animal or minerals can be hardly usedas a drug in their natural form. These substances are hard to use in their natural form, so they have to undergo some process prior to use to make them palatable and increase their efficacy. This process is termed as pharmaceutics that is *Bhaishajya Kalpana* in terms of Ayurveda. Ayurvedic Pharmaceutics (Rasa *shastra* & *Bhaishajya* Kalpana) offers many judicious processing techniques (*samskara*) to convert/modify these substances into different physical forms (dosage forms) withoutcompromising the palatability, safety and efficacy.[2] Different dosage forms are intended for internal as well as external use or in the diagnosis, treatment, mitigation or prevention of diseases or disorder in human beings or animals. All dosage forms are manufactured in exclusively accordancewith the formulae described in authoritative texts of Ayurvedic system of medicine specified in the first schedule of the drug and cosmetic act 1940.[3] Dosage form is a physical form of drug intended for administration or consumption by which the compounds are delivered into the sites of action within the body. Ayurvedic medicines can be classified into four categories based on their physical state as solid, semisolid, liquid and gaseous form. The Ayurvedic formulations range widely from freshly extracted plant juice to eye drops, ointments, surgical threads etc. However, there are five basic classical forms termed as '*Panchavidha kashaya'* from which all other drug formulations or forms are derived or developed. The five basic forms are:'*Swaras'* the expressed juice, '*Kalka'*, a fine paste obtained by grinding fresh or wet grinding dried plant material, '*Kwath'*, the decoction, '*Shita'* or '*Hima'*, the cold-water infusion and '*Fanta'*, the hot water infusion. The first two forms are prepared from freshly collected plant material and are directlyput to patient use, whereas the last three forms '*Kwath'*, '*Shita'* and '*Fanta'* are aqueous extracts prepared from the dried plant material.[4] *Bhaishajya Kalpana* also includes

preparation of variousforms of medicine such as *Churna*, *Guti*, *Vati*, *Ghrita Paka*, *Taila Paka*, *Lepa*, *Asava*, *Arishta*. etc. *Sneha Kalpana* is most commonly used Ayurvedic dosage form in day-to- day practice. These are preparations in which oil or ghee is boiled with prescribed *Kashaya's* (decoction), *Drava Dravya* like Milk, *Swaras* and *Kalka's* (fine paste) of drugs according to the formula. This process ensures absorption of the active therapeutic properties of the ingredients used, into the oil base. In thesepreparations three ingredients are essential- *Sneha* (ghee or oil), *Drava* (liquid)- which may be decoctions, expressed juice etc., and Kalka- the fine paste of the ingredients.[5]

As there are many of developments going on at present scenario in the field of the medicines, the Novel Drug Delivery System (NDDS) is also one of the results of these medicinal development. NDDSis combination of the advance techniques and the new dosage forms. NDDS refers to the formulation, systems and technologies for transporting a pharmaceutical compound in the body. Thus, different types of herbal NDDS are given Liposomes, Microspheres, Nano particles, Phystosomes, Transferosomes, Polymeric Micelle Formulation, Transdermal system, Implants, Micropellets, Complexation.[6] This review is an attempt to develop comparative view between Phytosomes and Sneha Kalpana and thus is development as novel dosage form.

MATERIAL AND METHODS

Sneha Kalpana (medicated oil/*Ghrita*)

Sneha Kalpana/*Paka* may be defined as "A pharmaceutical process to prepare oleaginous medicaments from the substances like *Kalka* (herbal paste of different parts of botanicals), *Kwath*(specifically prepared decoction in accordance of Ayurvedic principles) or *Drava Dravya* (any otherliquid such as milk, self-expressed juices, meat juice, etc.) taken in specific proportion and by subjecting them to unique heating pattern and duration to fulfil certain pharmaceutical parameters, according to the need of therapeutics.[7]*Kalka* (herbal paste), *Kwath* (decoction) or *Drava Dravya* (suchas milk, self-expressed juices, meat juice, buttermilk) are generally taken in proportion (1/4:1:4) and by subjecting them to unique heating pattern that is *Madaagni* and duration to fulfil certain pharmaceutical parameters.[8]

Preparation of *Kwath* for *Sneha Kalpana*

For the preparation of *Kwath*, according to hardness of *Kwathya dravya* (chopped herbs), water should be added for *Mridu dravya* (herbs of soft texture) four times, *Madhyama* dravya and *Kathina dravya* (herbs of harder texture) eight times, and *for Atyanta kathina dravya*

(most hard herbs)sixteen times, following rules are mentioned in the classics.[9]

Classification Of *Sneha Kalpana*[10]

Sneha Kalpana is classified into various categories based on different parameters. Those includes asfollows.

- Based on Nature of Media: *Ghrita, Taila, Vasa, Majja.*
- Based on source of *Dravya: Sthavar* (Plant Origin), *Janghama* (Animal Origin).
- Based on type of *Paka*: *Ama Paka, Mrudu Paka, Khara Paka, Dhagda Paka*.

Requirements For *Sneha Kalpana*

Sneha Kalpana needs the following constituents

1. *Kalka dravya*: Fine paste of medicinal plants and minerals should be taken as a *Kalka dravya*.
2. *Drava Dravya*: Water, *Kwath*, *Swaras*, *Kanji*, *Ksheer*, *Dadhi*, *Takra*, etc.
3. *Sneha Dravya*: Mainly different types of fat containing media such as *Taila* and *Ghee*.

Concept of Proportion Of Above *Dravya* In *Sneha Kalpana*

If the quantity of the ingredients is not mentioned, then the *Kalka*, *Sneha*, and *Drava Dravya* should be used in theproportion of 1:4:16, respectively. The ratio of Kalka, Sneha, and *Drava Dravya* mentioned inSharangadhar Samhita is given in Table 1.[11]

Table No 1.

RATIO OF KALKA DRAVYA, DRAVA DRAVYA, SNEHA DRAVYA ACCORDING TO SHARANGDHAR			
RATIO	**KALKA DRAVYA**	**SNEHA DRAVYA**	**DRAVA DRAVYA**
General	¼ th part	1 part	4 part
Specific	¼ th part	1 part	4 part (water)
	1/6 th part	1 part	4 part (Kwath)
	1/8 th part	1 part	4 part (Swarasa, Mansarasa, Dadhi, Ksheera, Takra)
	¼ th part	1 part	Up to 4 part
	¼ th part	1 part	More than four, all equal to Sneha

Methods Of Preparation Of *Sneha Paka*

Sneha Paka involves 3 processes

1. *Sneha Murchana*
2. *Sneha Paka*
3. *Sneha Siddhi*

***Sneha Murchana*[12]**

Before subjecting the drugs to *Sneha Paka*, *Sneha* is supposed to undergo one particular procedurecalled as *Sneha Murchhana*. It is applied for both *Taila* and *Ghrita*. It is considered as one of the Samskaras of *Sneha* and helps the *Sneha* to acquire specific pharmaceutical as well as therapeutic property. Bhaishajya Ratnavali is the first text, which described the importance and method of Murchhana process. Murchhana alters the solubility pattern and absorbability, which is desired to get maximum medicinal properties.

Objectives Of *Murchhana* Process

- *Amadosha* Haratwa - removal of "Ama" which can be correlated to the "moisture content"which can be directly related to rancidity problems.
- Removal of bad odour of crude Taila or Ghrita.
- Sneha will acquire the capability to receive more active principles.
- Stability of the Sneha is also supposed to increase.
- Impart appealing colour to the Taila.
- May alter the solubility and absorption of the finished product.

***Sneha Paka*[13]**

After *Sneha Murchana* of Tail and Ghrita, these Sneha dravya are subjected to Paka with as prescribed Kalka and Drava dravya. Moderate heat (*Manda Agni*) is given till the water portionget evaporated and only Sneha dravya is left which shows the signs of Sneha siddhi.

There are different opinions available regarding the method and time of addition of Kalka and Sneha during Sneha Paka. According to Sushruta Samhita and Astanga sangraha, Kalka and DravaDravya's are advised to mix in Sneha and processed. Acharya Sharangadhar did not specify the order in which the Drava, Sneha, and Kalka should be mixed. According to the Keraliya Vaidya's while preparing the Sneha Kalpana, first, the Kalka Dravya is mixed in Drava Dravya, then this mixture is poured in slightly heated Sneha and Sneha Paka is done. This will facilitate uniformdistribution of active principles in the Sneha.[14]

Sneha Paka Siddhi Lakshan

- Stoppage of crackling sounds in Sneha suggest no water Content in Sneha.
- Disappearance of bubbles in Ghrita and appearance of bubbles in Tail.
- Appearance of clarity in Tail.

- Kalka does not adhere to the fingers.
- Kalka attains perfect Varti shape when rolled between thumb and index.
- Kalka is neither very hard nor very soft.

Precautions While Preparing *Sneha Kalpana*[15]

Precautions that must be taken while manufacturing Sneha Kalpa for obtaining a good quality standard finished product are further classified into different stages.

1. Before the process

- The Sneha must be pure, clear, and without slurry.
- The Sneha should be taken after performing Murcchana samskara.
- The raw material used must comply with its identity, purity, and strength.
- Tail Patra should be wide-mouthed and of suitable size. Size of Sneha Patra depends on thebatch quantity and nature.

2. During the process

- *Madhya Agni* should be maintained throughout the process.
- The mixture should be stirred in the initial stage for facilitation of homogenous mixing andstirring in a later stage to avoid sticking of *Kalka* to the vessel resulting in carbonization.
- Care should be taken to determine the proper stage of *Sneha Paka*.
- If *Saindhava Lavana* and *Kshar Dravya* have to be added to Sneha, it has to be added toSiddha Sneha Kalpa and then filtered.
- If *Sarkara* is mentioned in the formula, then it should be added to the final product aftercomplete cooling.

3. After the process

- To obtain maximum yield, the finished *Sneha* should be filtered in hot condition itself.
- If *Sugandha Dravya* has to be added, then it should be added gently and carefully when the Sneha is in a lukewarm condition.

THERAPEUTIC USES OF *SNEHA PAKA*[16]

Table 2.

SNEHA PAKA	CHARAK	SUSHRUT	VAGHBAT	SHARANGDHARA
Ama Paka	No Therapeutic use	No Therapeutic use	No Therapeutic use	No Therapeutic use
Mrudu Paka	Nasya	Pana	Nasya, Pana	Nasya
Madhya Paka	Pana, Basti	Nasya, Abhyanga	Pana, Basti	All of the above
Dagdha Paka	Not Mentioned	Not Mentioned	No therapeutic use	No therapeutic use
Khara Paka	Abhyanga	Basti, Nasya	Abhyanga	Abhyanga

Therapeutic Uses Of *Sneha Kalpana*

Sneha Kalpa, that is, medicated oils/ghee of Ayurvedic dosage forms, are used in therapeutics both topically and systemically. Thus, we can see a wide variety of uses of Sneha Kalpana. Depending upontype of Sneha Paka their use as Topical or Oral dosage form changes. Nasya Kalpana (e.g., Sadabindu Taila, Anu Taila).

Mukha Kalpana (e.g., Irimedadi Taila)-Two types-Gandusha and Kawala Netra Kalpana-(e.g., Triphala Ghrita).

Abhyanga-(e.g., Dashamula Taila).

Anuvasana Basti-(e.g., Saindhavadi Anuvasana Taila) Uttar Basti, Pichu-(e.g., Mushakadya Taila).

Snehana in Panchakarma therapy-(e.g., Pancha Prasritiki Peya).

Internal administration-(e.g., Panchatikta Ghrita, Kshira Bala Taila) for shodhana/nourishment. In nonhealing ulcer-(e.g., Jatyadi Ghrita).

Now a days Medicated oils are used as Massage oils, Analgesic oils.

Basics of Novel Drug Delivery System

Novel drug delivery system is an approach to deliver Herbal drugs/ Traditional drugs in advanced dosage form. Basic advantage of NDDS is to increase efficacy, bioavailability of Herbal preparationand to reduce its side effects.

Modern Phytopharmaceuticals had shown promising benefits of fulfilling scientific needs like Pharmacokinetics, Mechanism of action, site of action, accurate dose of herbal preparation by theuse of NDDS such as Nanoparticles, Microemulsions, Phytosomes liposomes, solid dispersions, solid lipid Nanoparticles.

Basics Of Phytosomes

Phytosomes are recently introduced Herbal Formulations. These are gaining importance as

HerbalDrug and Nutraceuticals. It is formulation in which standardized plant extract or water soluble phytoconstituents are incorporated into phospholipids to produce lipid compatible complexes.[17] Phytosomes is term coined by two words Phyto – Plant and some – cell. These are also called as Herbosomes.[18]

This is a new patented technology, where standardized plant extracts or water soluble phytoconstituents are complexed with phospholipids to produce lipid compatible molecular complexes, there by greatly increasing absorption and bioavailability. Phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine, phosphatidylinositol are the phospholipids used, butphosphatidylcholine are widely used because of their certain therapeutic value in case of liver diseases, alcoholic steatosis, drug induced liver damage and hepatitis.[19] Phospholipids are alsoemployed as natural digestive aids and as carriers for both fat miscible and water miscible nutrients.[20]

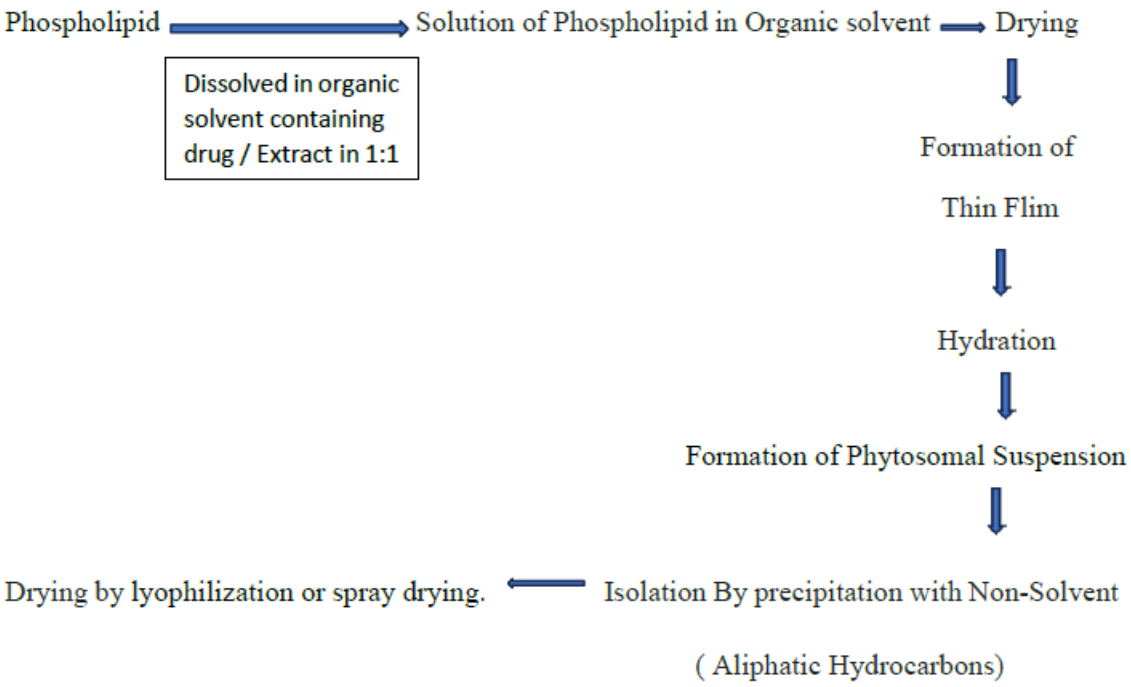
Structure Of Phytosomes

Phytosomes are complex of phospholipids and natural active phytochemicals, bound in their structures, obtained by the reaction between phosphatidylcholine (or any hydrophilic polar head groups) and plant extracts in an aprotic solvent; as shown in Fig 2.

Phytosomes are originated from the reaction of a stoichiometric quantity of the phospholipid (phosphatidylcholine) with polyphenolic constituents or standardized extracts (flavonoids, tannins, terpenoids, xanthones) within a non-polar solvent. The lipid-soluble phosphatidyl portion completelycovers the hydrophilic phytoconstituent-choline complexes. chemical bonds are formed among the polar head of the amphiphile molecule and phytoconstituent.

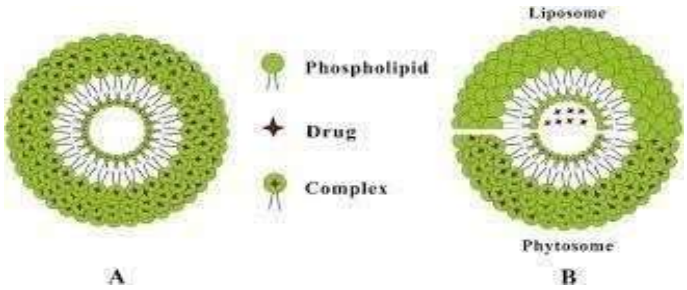
Preparation Of Phytosomes[21]

Phytosomes are prepared by reacting 3–2 moles (preferably with one mole) of a natural or syntheticphospholipid, such as phosphatidylcholine, phosphatidyl- ethanolamine or phosphatidylserine, withone mole of phytoconstituents either alone or in the natural mixture in an aprotic solvent, such as dioxane or acetone, in a 1:2 or 1:1 ratio. The optimum ratio of phospholipid to phytoconstituent is 1:1. The complex thus formed can be isolated by precipitation with an aliphatic hydrocarbon or lyophilization or spray drying.



Flow chart Representation of Preparation of Phytosomes

(Fig 1)



(Fig 2)

Phytosomes Structure

Properties Of Phytosomes

Physico-chemical properties[22]

- The spectroscopic data reveals that the phospholipid- substrate interaction is due tothe formation of hydrogen bond between the polar head (i.e., phosphate and ammonium group) and the polar functionalities of the substrate.
- The size of Phytosome varies from 50 nm to a few hundred µm.
- Phytosomes when treated with water, they assume a micellar shape resemblingliposome and Photon Correlation Spectroscopy (PCS) reveals these liposomal structures acquired by Phytosomes.

Biological Properties[23]

Phytosomes are advanced forms of herbal products that are better absorbed, utilized and asa result produce better results than conventional herbal extracts. The increased bioavailability of the Phytosome over the non-complexed botanical derivatives has been demonstrated by pharmacokinetic studies or bypharmacodynamics tests in experimentalanimals and in human subject.

Mechanism Of Action Of Phytosomes

Phytosomes are formed by using water soluble plant extracts (which are less easily absorbed due toinstability) or water and lipid soluble phytoconstituents. Some of these phytoconstituents despite showing therapeutic activity invitro they show less in vivo actions due to improper molecular size, poor absorption in lipids poor bioavailability which are major limiting factors for molecules to pass the biological membrane and to absorbed systematically by taking orally or topical administration. Phospholipids are employed as natural digestive aid and as carrier for both water and lipid miscible nutrients. Phytosomes are considered as targeted Drug delivery system thus shows activity on propersite of action.[28]

Phytosomes can transverse the lipophilic path of the enterohepatic cell membranes and also stratumcorneum layer of skin. Phytosomes also enhances Bioavailability of phyto - constituents through GI tract.

Advantages Of Phytosomes[24,25,26,27]

1. Phytosomes produces a little cell where the important components of herbal extracts areprotected from destruction by gut bacteria and digestive secretions.
2. It assures proper delivery of drug to the respective tissues.
3. The safety of the nutrients of the herbal extract is not been compromised by conveying theherbal drug as means of phytosomes.
4. As the absorption of active component is improved, its small dose can produce desiredresults.
5. The bioavailability of drug is enhanced remarkably.
6. Efficiency of entrapment is high and more over predetermined because drug itself is inconjugation with lipids in forming vesicles.
7. Formulation is easy as there is no problem in drug entrapment.
8. Phytosomes shows better stability due to the formation of chemical bonds betweenphytoconstituents and the Phosphatidylcholine molecules.

9. Besides acting as a carrier Phosphatidylcholine used in formulating Phytosome process alsonourishes the skin as it is an important part of a cell membrane.
10. Phytosomes are more useful than liposomes in skin care products.
11. Phytosomes have significantly greater clinical benefit.
12. Besides acting as a carrier Phosphatidylcholine used in preparation of phytosomes also actsas a hepatoprotective resulting in synergistic effect when hepatoprotective substances are employed.
13. They are less soluble in aqueous media which allows the formation of stable emulsions orcreams.

DISCUSSION

Most of the bioactive constituents of phytomedicines are water-soluble molecules (e.g., phenolics, glycosides, and flavonoids). However, water soluble phytoconstituents are limited in their effectiveness because they are poorly absorbed when taken orally or when applied topically. Herbal Phyto molecules are poorly miscible with oils and other lipids and often fail to pass through the smallintestine because of its lipoidal nature. The effectiveness of any herbal product is dependent upon delivering an effective level of the active compounds.

Phytosomes Novel drug delivery system showspromising result in enhancing Bioavailability, greater clinical benefits without compromising Nutrient Safety. Water Soluble Phyto molecules (flavonoids, polyphenols, etc) can be converted intolipid friendly complexes by reacting herbal drugs with phospholipids thus forming Phytosomal complex. These complexes can cross the lipid-rich bio membranes and, finally, reach the blood. Theyhave improved pharmacokinetic and pharmacological parameters which are advantageous in the treatment of acute diseases as well as in pharmaceutical and cosmetic compositions.

Phytosomes are made of phospholipids which are natural digestive aid thus increasing activity of digestive enzymes. It also acts as a carrier for both water and fat soluble phytoconstituents. This activity of Phospholipids can be compared with Traditional *Ghrita* in Ayurveda. According to Ayurvedic classics *Ghrita* has a property of Samskara Anu Vartan (it carries all properties of other drugs along with its own properties and potency. It is absorbed in all Sukshma strotas of the body). and Deepan Properties. Thus, Phospholipids can be compared with Ghrita.

Various *Ghrita Kalpana* prescribed for therapeutic uses can be thus developed as phytosomes. Thesedosage form will help us to develop details about mechanism of *Ghrita*

prescribed in various diseases thus generating information on Pharmacokinetic and Pharmacodynamics of Drugs. In Ayurveda Treatment of *Manas Roga* basically focuses on suppression of excess *Vata* thus has importance of *Ghrita Kalpa's* in its treatment. These Ghrita Kalpana if developed into Phytosomes complexes due nano particle size they can cross Blood brain barrier and thus shows effect on functions of Brain, for further confirmation of these studies Blood compatibility study has to be done.

Phytosomes can be formulated as Soft Gelatine capsules. The Phytosomes complex can be dispersedin oily vehicles to obtain suspensions to be filled in soft gelatine capsules. These capsules are most suitable vehicle for Phytosomes complexes and thus increases palatability of Sneha Kalpana and stability while transportation.

Phytosomes can be formulated as topical dosage forms in the in the form of emulsions of oil in water or water in oil. Traditionally lepa was topical dosage form but due to its less stability and difference inwater or Ghrita (act as carrier for herbal powder preparation) percentage from patient to patient itstherapeutic effect was hampered. These drawbacks can be overcome.

Phytosomes has advantage over liposomes in terms of bonding between phospholipid and phytoconstituents In which Phytosomes possess hydrogen bonds between the two thus formingstable compound where as in liposome phytoconstituents are freely present in central cavity ofcomplex. Phytosomes are better for oral drug delivery because of increased bioavailability.

However, there are certain limitations in this review regarding proper detailed mechanism on howthese Phytosomes work or what are the main sites of action, In vivo and Invitro studies of these dosage form can developed literature on this.

CONCLUSION

Sneha Kalpana is process of heating water soluble Drugs in the form of Kwath or Kalka with Sneha thus making various more potent siddha Sneha as per their therapeutic uses. Sneha dravya are also use as carrier in various lepa or topical preparation like Nasya, Abhyanga. Topical Application like lepauses water as base for application of herbal drugs. Phytosomes are phospholipids compounds that provide better absorption, increased bioavailabilityof water and lipid soluble herbal extracts. Due to these properties Sneha Kalpana can be given as novel

dosage system in th form of Phytosomes. Liposomes are also phospholipid compounds but Phytosomes are more stable and more absorption when taken orally or applied topically due topresence of hydrogen bonds between phytoconstituent and polar head of phospholipid. This formulation methodology of Phytosomes can be easily upgraded to a commercial scale. Thus, *SnehaKalpa* can be converted to more stable, easily made on large scale and increase bioavailability and palatable dosage form. Presently Phytosomes are used primarily in cosmetics to deliver water soluble substances to the skin. The technology can effectively deliver the product by topical and oralroute. Phytosomes of Sneha Kalpna or Kwath Kalpana can be formulated as soft gelatine Capsule, Hard Gelatine Capsules, tablets and Topical dosage form.

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