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Ayurveda

GHRITA AS A TRADITIONAL LIPID-BASED DRUG DELIVERY SYSTEM: A REVIEW OF SNEHA KALPANA, BIOAVAILABILITY AND POTENTIAL RELEVANCE TO GARBHINI PARICHARYA

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ABSTRACT Oral bioavailability is a major challenge in the delivery of poorly water-soluble phytoconstituents and therapeutic compounds. Contemporary lipid-based drug delivery systems (LBDDS), including self-emulsifying drug delivery systems (SEDDS), self-micro emulsifying drug delivery systems (SMEDDS), solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs) and liposomes, enhance drug solubilisation and absorption through lipid-mediated gastrointestinal and, for selected compounds, lymphatic transport. Ayurveda describes an established pharmaceutical methodology, Sneha Kalpana, in which medicinal substances are processed with lipid media such as Ghrita and Taila. This review explores the pharmaceutical and mechanistic parallels between Ghrita prepared by Sneha Kalpana and contemporary lipid-based drug-delivery systems, with consideration of its potential relevance to Garbhini Paricharya and the delivery of selected Ayurvedic phytoconstituents during pregnancy.

KEYWORDS : Ghrita, Lipid-based Drug Delivery Systems, Oral Bioavailability, Phytoconstituents, Garbhini Paricharya, Maternal–foetal Drug Delivery.

INTRODUCTION

Oral bioavailability remains one of the central challenges in pharmaceutical formulation. A considerable proportion of contemporary drug candidates exhibit inadequate aqueous solubility and/or permeability, resulting in dissolution- or absorption-limited oral bioavailability. The Biopharmaceutics Classification System (BCS) categorises compounds according to aqueous solubility and intestinal permeability, with BCS class II and class IV compounds presenting formulation challenges. Lipid-based drug delivery systems (LBDDS), including self-emulsifying drug delivery systems (SEDDS), self-micro emulsifying drug delivery systems (SMEDDS), solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs) and liposomes, have consequently been developed to improve solubilisation, intestinal absorption and, for selected lipophilic compounds, lymphatic transport.[1-6]

Lipid-based formulations can enhance oral absorption through several mechanisms, including incorporation of poorly water-soluble compounds into a lipidic vehicle, improvement of drug solubilisation within the gastrointestinal milieu, stimulation of endogenous lipid digestion and lipoprotein formation, alteration of enterocyte drug disposition, and promotion of intestinal lymphatic transport. Importantly, lymphatic transport is formulation- and molecule-dependent and is particularly relevant to sufficiently lipophilic compounds capable of associating with chylomicron pathways; it should therefore not be regarded as an obligatory route for all lipid-based formulations.[3-6]

Ayurveda had developed an elaborate pharmaceutical methodology for processing medicinal substances with lipid media under the broader concept of *Sneha Kalpana*. Within this pharmaceutic group, *Ghrita* (medicated ghee) and *Taila* (medicated oil) are prepared by processing a lipid base with herbal paste (*Kalka*) and a liquid component such as decoction (*Kashaya*) or another prescribed liquid medium (*Drava Dravya*). Classical Ayurvedic pharmaceutics describes characteristic stages and endpoints of *Sneha Paka*, indicating that the process is not simply an infusion of herbs into fat but a controlled pharmaceutical operation with recognisable organoleptic and physicochemical endpoints.[7-10]

The classical concept of *Sneha Kalpana* has attracted comparison with modern lipid-based delivery technologies because both approaches employ a lipid phase to facilitate the incorporation and subsequent administration of medicinal substances. Such comparisons, however, are best understood as functional or conceptual analogies.

The relevance of *Ghrita* becomes particularly interesting in the context of *Garbhini Paricharya*, the Ayurvedic antenatal regimen described in the classical literature. Several classical sources describe the use of *Ksheera*, *Ghrita* and other dietary preparations during pregnancy, with the third month specifically associated in *Charaka* and related traditions with *Ksheera* combined with *Madhu* and *Ghrita.*[12-14]

Pregnancy provides a scientifically relevant context for studying lipid-mediated nutrient and drug transport. Maternal long-chain fatty acids are actively handled by the placenta, and the syncytiotrophoblast expresses multiple fatty-acid transport and binding proteins. Docosahexaenoic acid (DHA) undergoes preferential placental transfer and is important for foetal development.[15-18] This established physiology provides a plausible biological basis for investigating whether lipid-associated phytoconstituents might demonstrate altered maternal disposition or placental exposure.

Mechanistic Foundations of Ghrita as a Lipid-Based Delivery Matrix

Snehana and the pharmaceutical concept of lipid-mediated delivery

Snehana (oleation) is a major therapeutic and preparatory concept in Ayurveda, and Ghrita is one of the principal internal oleaginous media. Classical Ayurvedic descriptions attribute specific physiological properties to unctuous substances and describe their interaction with body tissues and channels (*Srotas*).

Modern pharmaceutics treats lipids as vehicles for drug delivery because they improve solubility of hydrophobic compounds, facilitate lymphatic transport and enables modulation of absorption kinetics.[19] From a modern pharmaceutical perspective, A lipid vehicle can alter the physicochemical environment surrounding a poorly water-soluble compound and thereby influence dissolution, digestion, micellar solubilisation and intestinal absorption. Lipid digestion produces fatty acids and monoacylglycerols that interact with bile salts and phospholipids to generate colloidal structures capable of maintaining lipophilic compounds in an absorbable state.[3-6]

Accordingly, the relevance of *Ghrita* as a drug-delivery matrix can be considered at several levels:

- Extraction or incorporation of selected phytoconstituents into the lipid phase during pharmaceutical processing;
- Modification of gastrointestinal solubilisation after oral administration;
- Interaction with endogenous bile and digestive processes
- Potential contribution to lymphatic transport for sufficiently lipophilic constituents.

Taila and *Ghrita* can be conceptualized as traditional lipid vehicles with unique processing-induced properties (herbal-derived surfactants / bio capping, Maillard / thermal transformation products) that influence pharmacokinetics and pharmacodynamics.[20,21]

Sneha Paka and Pharmaceutical Processing

During *Sneha Paka*, *Ghrita* is processed with *Kashaya* and *Kalka* under controlled heating and stirring. Classical pharmaceutical texts describe defined proportions and *Paka Lakshanas* for determining completion of the process. The commonly described general ratio of *Sneha:Drava:Kalka* is approximately 1:4:1 by volume/weight conventions depending on the formulation and classical source, although individual preparations may prescribe different proportions.[7-10]

The Ayurvedic Pharmacopoeia of India provides modern pharmacopeial standards for selected *Ghrita* and *Taila* preparations and recognises physicochemical and analytical quality-control procedures relevant to Ayurvedic formulations.[10]

Table 1. Classical stages of *Sneha Paka* and their pharmaceutical interpretation

Paka Stage	Classical Pharmaceutical Status	Contemporary Interpretation
Ama Paka	Incompletely processed Sneha with inadequate completion of the process	May indicate inadequate removal of aqueous phase and incomplete incorporation of constituents; requires further processing
Mridu Paka	Softer endpoint with comparatively softer Kalka	Traditionally preferred for selected applications, particularly Nasya and other contexts requiring a softer preparation
Madhyama Paka	Intermediate/optimal endpoint for many internal preparations	Commonly regarded as the appropriate endpoint for many oral Sneha preparations, subject to the individual formulation
Khara Paka	More advanced heating with hard/brittle Kalka	Traditionally associated mainly with external applications; excessive heating may alter heat-sensitive or volatile constituents

Modern analytical studies have attempted to correlate classical *Paka Lakshanas* with physicochemical parameters, chromatography and other instrumental measurements, supporting the possibility of developing reproducible quality-control markers for Sneha Kalpana.[9,22]

The pharmaceutical importance of the heating process is therefore potentially twofold: it facilitates transfer of selected constituents between aqueous and lipid phases and simultaneously determines the final physicochemical characteristics and stability of the preparation. However, the exact partitioning of individual phytoconstituents during *Sneha Paka* remains formulation-specific and requires analytical validation.

Ghrita and Modern Lipid-Based Drug Delivery Systems

The composition and behaviour of *Ghrita* permit useful comparison with several modern LBDDS, but the comparison should be made at the level of pharmaceutical function.

Table 2. Functional comparison between *Ghrita* and contemporary lipid-based delivery systems

Pharmaceutical Feature	Possible Mechanism in Ghrita	Relevant Modern LBDDS Concept
Lipidic Solubilisation	Incorporation of selected lipophilic or amphiphilic constituents into the lipid phase	SEDDS/SMEDDS; lipidic solutions
Enhanced Gastrointestinal Solubilisation	Digestion of dietary lipids and interaction with bile-derived colloidal structures	Lipid-based oral formulations
Potential Lymphatic Transport	Applicable principally to sufficiently lipophilic constituents associated with chylomicron-mediated transport	SEDDS and other lymphatic-targeting lipid systems
Protection/Alteration of Chemical Environment	Lipid matrix may influence degradation and release of selected constituents	Lipid nanoparticles and liposomes
Controlled Physicochemical Release	Dependent on lipid composition, digestion and constituent partitioning	SLNs/NLCs and other lipid matrices
Membrane Interaction	Lipid digestion products and amphiphilic molecules may influence intestinal membrane interactions	Liposomes and lipid nanocarriers

Modern literature demonstrates that lipid-based formulations can enhance the oral absorption of poorly water-soluble compounds through solubilisation, interaction with bile and pancreatic digestion products, and in selected cases, intestinal lymphatic transport.[1-6]

Potential Relevance to *Garbhasthapaka Dravyas*

Garbhasthapaka Dravyas constitute an important conceptual group within Ayurvedic discussions of pregnancy and preservation of gestation. Herbs such as *Shatavari* (*Asparagus racemosus*) and other *Madhura* or pregnancy-associated drugs are described in various classical and later Ayurvedic textbooks.[12-14]

From a modern phytochemical perspective, *Asparagus racemosus* contains steroidal saponins, including Shatavarins, as well as flavonoids and other secondary metabolites.[23,24] *Withania somnifera* contains steroidal lactones collectively referred to as withanolides.[25] The presence of these chemically diverse constituents provides a reasonable basis for investigating whether the pharmaceutical vehicle influences their extraction, stability and systemic exposure.

Enhanced extraction efficiency

The proposition that a lipid phase can preferentially incorporate lipophilic constituents is consistent with basic principles of solvent partitioning. However, not all steroidal saponins are simply "fat soluble"; their amphiphilic glycosidic structures may exhibit complex partitioning behaviour.

Comparative studies using validated analytical techniques such as HPLC, HPTLC and LC-MS/MS determine the concentration of marker constituents in the starting material, aqueous phase, lipid phase and final *Ghrita.*

Digestion-mediated release

A second possible mechanism concerns the fate of lipid-associated compounds following oral administration. Dietary triglycerides undergo digestion by gastric and pancreatic lipases, while bile salts and phospholipids facilitate the formation of mixed micellar and other colloidal structures. These processes can increase the apparent solubilisation of lipophilic compounds and alter their intestinal absorption.[3-6] Therefore, During the consumption of *Ghrita*, lipid digestion modifies the rate and extent of liberation and absorption of incorporated phytoconstituents.

Placental Transport and Foetal Exposure

The placenta is a highly specialised transport and metabolic organ rather than a nonspecific lipid-permeable barrier. Maternal fatty acids cross the syncytiotrophoblast through a combination of passive and protein-mediated processes involving fatty-acid transport proteins and intracellular binding proteins.[15-18]

DHA is of particular importance because the developing foetal brain requires substantial quantities of long-chain polyunsaturated fatty acids, particularly during later gestation. Placental transport mechanisms contribute to preferential delivery of DHA and other long-chain polyunsaturated fatty acids to the fetus.[16-18]

These findings establish that lipid-associated nutrients can undergo regulated maternal–placental–foetal transfer. Thus, *Ghrita* could alter foetal exposure to selected lipophilic phytoconstituents is therefore biologically plausible. Direct demonstration would require:

1. Quantitative characterisation of the phytoconstituents in the Ghrita;
2. Maternal pharmacokinetic studies
3. Measurement of placental tissue concentrations

4. Assessment of foetal exposure in an appropriate experimental model
5. Placental transport studies using validated in vitro or ex vivo systems
6. Maternal and foetal safety assessment.

Impact On Maternal and Foetal Outcomes

Maternal Nutritional and Metabolic Considerations

Ghrita is an energy-dense dietary lipid and can contribute to dietary energy intake. Dietary lipids are important during pregnancy because maternal energy requirements and the requirements for essential fatty acids increase as pregnancy progresses. Maternal dietary fatty-acid status also influences the availability of long-chain polyunsaturated fatty acids to the placenta and fetus.[17,18,26] The evidence of diet which is mentioned in *Garbhini Paricharya* being predominantly ghee rich, shows that that supplementation of all essential fatty acids mainly DHA (Docohexanoic Acid) during gestation, which otherwise is available only by consumption of sea foods.

The consumption of *Ghrita* is observed to improve maternal or foetal outcomes, by considering the required amount, dietary context, total energy intake, metabolic status and the composition of the remainder of the maternal diet.

Gut–brain axis and short-chain fatty acids

Butyrate and other short-chain fatty acids (SCFAs) are important microbial metabolites involved in intestinal barrier function, immune signalling and gut–brain communication. Butyrate acts through mechanisms involving G-protein-coupled receptors and histone-deacetylase inhibition.[27,28]

Foetal Development and Neurodevelopment

Long-chain polyunsaturated fatty acids, particularly DHA, have important structural and functional roles in foetal neural development. Placental transfer of DHA increases in importance during pregnancy, with substantial foetal accumulation occurring during later gestation.[16-18,26] These observations provide a biological rationale for investigating maternal dietary lipid quality during pregnancy. Therefore, the nutritional lipid content of the maternal diet contribute to the substrate available for placental and foetal lipid metabolism.

Uterine Quiescence and Preterm Labour

Prostaglandins are important mediators of the transition from pregnancy-associated uterine quiescence to labour, and changes in prostaglandin synthesis, metabolism and receptor signalling occur during parturition.[29,30]

DISCUSSION

The present review proposes that *Ghrita* prepared according to the classical principles of *Sneha Kalpana* may be regarded as a traditional lipid-based pharmaceutical matrix with potentially relevant parallels to contemporary lipid-based drug-delivery systems. The comparison is supported at the level of pharmaceutical principles: both systems exploit lipid phases to modify the solubilisation, digestion and absorption behaviour of selected compounds.[1-6]

The classical pharmaceutical process of *Sneha Paka* further demonstrates that Ayurvedic pharmaceutics incorporated defined processing steps and observable endpoints. Classical descriptions of *Mridu*, *Madhyama* and *Khara Paka*, together with contemporary analytical studies of *Sneha* preparations, suggest an opportunity to correlate traditional pharmaceutical observations with modern physicochemical parameters.[7-9,20]

The comparison between *Ghrita* and SLNs, NLCs, SEDDS/SMEDDS and liposomes is similar and can be expressed as a functional analogy. Modern LBDDS are engineered systems with specific compositions, particle sizes, interfacial properties, release profiles and pharmacokinetic characteristics.[1-6,11,31] The scientific interest of *Ghrita* lies instead in the possibility that traditional processing generates a complex lipid–phytochemical matrix capable of influencing extraction, digestion and absorption.

The proposed relationship between *Ghrita* and *Garbhasthapaka Dravyas* is particularly important. *Shatavari* contains steroidal saponins, while *Ashwagandha* contains withanolides and other bioactive constituents.[23-25] Lipid-based processing may influence the extraction and disposition of such compounds, but this requires formulation-specific analytical and pharmacokinetic evidence.

The placental transport literature provides an important mechanistic context. Maternal fatty acids, particularly DHA and other long-chain polyunsaturated fatty acids, undergo regulated uptake, metabolism and transfer across the placenta.[15-18] This establishes a biological basis for maternal–foetal lipid transfer.

Recent research has begun to investigate *Ashwagandha* root preparations in pregnant populations.[25,32]

Ghrita may represent an interesting traditional lipid-based matrix whose pharmaceutical behaviour can be investigated using modern formulation science. The most important research questions include phytoconstituent partitioning during *Sneha Paka*, lipid digestion, intestinal permeability, lymphatic transport, pharmacokinetics, placental transfer and maternal–foetal safety.

Future investigations should therefore combine Ayurvedic pharmaceutical standardisation with contemporary analytical and pharmacokinetic methodology. Comparative studies of aqueous extracts, conventional *Ghrita* and experimentally characterised lipid-based formulations could determine whether *Sneha Paka* produces measurable changes in marker-compound concentration, dissolution, digestion-dependent solubilisation, systemic exposure and tissue distribution.

CONCLUSION

Ghrita prepared through *Sneha Kalpana* represents a distinctive traditional Ayurvedic pharmaceutical system in which medicinal substances are processed with a lipid vehicle under defined classical conditions. Contemporary pharmaceutical science provides several plausible mechanisms through which lipid matrices can influence the solubilisation and absorption of poorly water-soluble compounds, including enhanced gastrointestinal solubilisation and, for selected lipophilic molecules, intestinal lymphatic transport.

The available evidence supports a functional analogy between Ghrita and modern lipid-based drug-delivery approaches. Similarly, placental transport of maternal fatty acids provides biological plausibility for studying lipid-associated phytoconstituent transfer.

The relationship between *Ghrita, Garbhasthapaka Dravyas* and *Garbhini Paricharya* therefore represents a promising translational research area. Future studies should integrate classical Ayurvedic pharmaceutical parameters with modern chromatographic characterisation, lipid-digestion models, intestinal permeability assays, pharmacokinetic studies, placental transport models and appropriately designed maternal–foetal safety studies.

The scientific significance of *Sneha Kalpana* recognises that Ayurvedic lipid pharmaceutics provides a historically established medicinal matrix whose formulation principles can be investigated using contemporary drug-delivery science.

Ghrita represents a scientifically relevant traditional lipid-based pharmaceutical matrix and provides an important interface between Ayurvedic pharmaceutics and contemporary drug-delivery science. Its potential to modify phytoconstituent bioavailability warrants systematic investigation using chromatographic characterisation, lipid-digestion models, intestinal permeability studies, pharmacokinetic assessment and placental transport models. Integrating classical pharmaceutical parameters with modern formulation science may provide a rigorous translational framework for evaluating *Sneha Kalpana* and its potential applications in pregnancy-associated Ayurvedic formulations.

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