



Science Behind *Ghrita* - The Lipid-Based Ayurvedic Formulations

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Introduction

Ghritas are Ayurvedic formulations, identified as *Herbal Ghee* in the modern context, meaning the concoction of clarified butter (*ghrita* or ghee) with aqueous decoction of herb and powdered or processed crude drugs in the lipidic ghee (clarified butter), singly or in combination, as per requirement [1].

Ayurved extensively uses this bovine lipidic vehicle, ghee (clarified butter) amongst major types of lipidic bases (*Maha Sneha*)- *Ghrita* (clarified butter), *Talia* (oil), *Vasa* (animal fat) and *Majja* (bone marrow of animals) mentioned as per the Text *Ashtang Hrudaya Sutrasthana*. Early descriptions of *ghritas* as nutritive agents (*rasayanas*), for daily use to increase longevity are found in the text *Charaka Samhita* [2]. The qualities of *ghrita* as a substance for use, was established in the *Upanishad* and *Sushruta* period. Later, the *Bhavaprakasha* mentioned *Ghrita* as *Yogavahi Rasayana*, i.e. an agent capable of acquiring and imparting the entire quality of “drug” added to it [3,4].

There are sufficient studies suggesting that ghee-based dosage of herbal drugs, extracts, their derivatives, have enhanced efficacy in contrast to usage as powder or tablet form [5]. The present communication aims to discuss the scientific reasoning behind the age-old clinical usage of the *Ghritas* and to extrapolate it to modern lipid soluble dosage forms.

Modern LBDDS have evolved largely to address challenges like solubility and bioavailability of poorly soluble drugs. They have proved to be attractive candidates for the formulation of pharmaceuticals, as well as vaccines, diagnostics, and nutraceuticals. Lipid-based formulations are easily tailored to meet a wide range of product requirements dictated by disease indication, route of administration, cost consideration, product stability, toxicity, and efficacy. Novel LBDDS claims to be advantageous w.r.t the versatility of excipients use, versatility of the formulations, stability, enhanced drug content, feasibility of carrying both lipophilic and hydrophilic drugs, and ‘ready-to-market type’ passive non-invasive formation of vesicular and non-vesicular system [6].

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Ghritas-The Lipid Based Formulations *Ghritas* are long-used medications available in various dosage forms and inscribed in the ancient texts as Ear drops (*Karnapoorana*), Massage (*Shata Dhatua Ghrita for reducing internal and burning sensation*), Wound healing (*Jatyadi Ghrita*), Hair Care, Enema, and Oral consumption.

Ghritas are known to be in higher congenity to the human body, at every stage of life from infant, pediatric, Adult i.e. a Man’s or Woman’s body and Geriatric state and hence are suggested for growth and longevity (*Rasayana Therapy*). Therapies are further redefined with different routes for administration of *ghrita* like *Snehapana* for oral administration; *Sneha Kalpa* is the form of therapy for external topical applications (*Lepa*), Nasal application (*Nasya*), Enema and eye application.

The *Ghrita* and LBDDS as oral forms are absorbed from GIT yielding a solubilized solid-state solution with micronized particles. They further bio-distribute by altering electrolyte-based transport system, drugs uptake, efflux and disposition *via* further stimulating the intestinal-lymphatic system. The avoidance of the first-pass metabolism and targeting specific diseases makes LBDDS a good candidate for newer drugs. Further, digestion of triglycerides is initiated by gastric lipases, forming micro emulsions, which are broken to diglycerides, monoglycerides and finally to free fatty acid. The lipid-based formulations have better bioavailability without being affected by food. Further the systemically circulating lipid *via* oral or external administration easily passes the blood brain barrier by- (1) lipid-mediated free diffusion through the BBB or (2) carrier- or Receptor-Mediated Transport (RMT) through the BBB. *Ghrita* being a complex fat rapidly crosses the BBB and makes the drug available in the CNS.

Like any other LBDDS with lipidic core, *Ghrita* serves as a vehicle and excels as a therapeutic agent by reaching all the organs and tissues within a short duration, without any alteration of the drug. So, the use of *Ghrita* in drug delivery is not a new trend now, but still is a promising concept [6,7].

Ghritas as Vehicle

Ghrita as an excipients with approx 98% of lipid and up to 1% of moisture, is easy to digest, solubilize, assimilate, stable, sweet and has flavors [7]. The fatty acids (triglycerides) contribute to *Ghrita*'s physical, organoleptic; bio-distribution and nutritional property are listed by FDA as most common excipients with GRAS (Generally Recognized as Safe) status. The unique ratio of triglycerides and processing make *Ghrita* lesser prone to rancidity by lipolysis while the unsaturated fatty acid like oleic acid is protected by natural antioxidants, Vitamin A and Vitamin D. Levels of phospholipids and moisture are indicative of stability to microbial spoilage and oxidation providing *Ghritas* a fairly better shelf life. Moreover, *Ghritas* are non-allergic and non-irritant, unlike certain plant-based oils *viz.* Mustard or Sesame.

Furthermore, *Ghrita* as a vehicle incorporates water soluble components like phenolics from herbal juices or lipid soluble components like high molecular weight alkaloids or terpenoids simultaneously making it an excellent therapeutics agent, complying with the principle objective of enhanced bioavailability and solubilization.

Processing of the Vehicle Ghrita

Commercially, *Ghrita* as a vehicle is prepared directly from the cream or butter, directly or by separating the butter in cold temperature and then heating to yield a food grade nutritive substance. But the texts of *Bhaishajya Ratnavali* emphasize on fermentation of cream or addition of curd to get butter processing. Further, this butter clarified by heating, enriches *Ghrita* with DHA (decohexanoic acid), a long chain PUFA (Polyunsaturated Fatty Acid) [8].

Processing *Ghrita* also includes purification (*Ghrita murchana*) on mild fire till, with listed herbs e.g. myrobalans, turmeric, *Cyperus* and lemon helping it improve and make it more digestible. The purified thermo-oxidized stable *Ghritas* are used to prepare potent formulations. Simple technique of addition of the polar phytoconstituents from herbal juices and non-polar phytoconstituents *via* heating, forms micronized and homogeneous dispersion of drug, which even on long term storage does not separate [9].

Interestingly, Ayurveda believes in processing of a substances based on time, where the substances transform itself with aging like *Guggul (Commiphora mukul)*, *Bhallatak (Semicarpus anacardium)*, *Guda (Jaggary)* and *Ghee (Ghritam)* [10,11]. Further, these texts also see the differences in the utilization of the *Ghrita* according to the time-based processing and confers the saying "Older the Ghee, more capable it is to balance the three Doshas (humors)- Vata (air), pitta (fire) and Kapha (body fluid/phlegm), Better is its quality" [11].

According to the Bhavaprakasha, categories available for *Ghritam* as per their Age are - *Purana ghritam* (1 year old), *Parpurana ghrita* (10-year-old), *Kumbha Ghritam* (100 years old). Furthermore, the *Susharata* identifies, 111-year-and *Ghritam* as *Kumbha Ghritam* and any *Ghrita* older than this was termed as *Maha Ghritam*. Rathi in 2018, established this belief of superior quality and better therapeutics of Aged *Ghrita* (15 years old *Purana Ghrita*) with the *Fresh Ghrita*

with its comparative fatty acid profiling. Studies further establish that enrichment of diglycerides; monoglycerides and free fatty acids vary due to breakdown of triglycerides by hydrolysis during aging of *Ghrita* [12].

The entire method of processing the *Ghrita* is in consensus with present framework of performance of Lipid based formulation, wherein the ratios of excipients, surfactants and co-solvent help to attain the digestibility, dissolution of the formulation in accordance with the adopted Lipid Formulation Classification (LFS), 2006 [10,12].

What is the Gross Composition of Ghrita and why is it the Preferred Source?

Ghrita formulations are prepared from ghee obtained from animal-based fat. Though the literatures from Ayurved mentions some 8 sources for ghee *viz.* Cow, Goat, Sheep, Buffalo, Camel etc. but cow ghee is the most preferred among all as it is excellent for balancing Vata (air) and Pitta (fire) related doshas (humors). This could be attributed to the variation in the lipid content in correlation to the difference of source. Other *ghritas* under consideration is Buffalo *ghrita*, preferred as a substitute to cow ghee. Goat *Ghrita* too, are used in certain specific formulations like for eye disorders e.g. Anantaadi Aja-*Ghrita* [13,14].

The gross composition constitutes of triglycerides (\cong 98%), with traces of diglycerides (1% to 2%), monoglycerides (0.1% to 0.2%), free fatty acids (1 mg/100 mg to 10 mg/100 mg), phosphosphingolipids (0 mg/100 to 80 mg/100, sterols (mainly cholesterol), fat soluble vitamins, carbonyl (4 ug/g to 6 ug/g), glyceryl ethers (0.8 uM/g) and alcohols (1.82.3 uM/g to 2.3 uM/g) [15,16].

The total fatty acid fraction of cow *ghrita* can be categorized based on the no of double bonds namely as (1) Saturated Fatty Acids (SFA) - without double bonds, up to 46% to 47.8%; (2) Unsaturated Fatty Acids (USFA) constituting up to - 36% of Monounsaturated Fatty Acid (MUFA) and 18% of Polyunsaturated Fatty Acid (PUFA); (3) a significant quantity of ruminant Trans-Fatty Acids (rTFA) [17]. The higher percentage of USFA is attributed with the therapeutic property of cow *ghrita*, an excellent *Panchgavya* (product from cow) [18].

Further, cow *ghrita* being a rich of short chain fatty acid (SCFA, <C6), butyric acid obtained by conversion of fiber by the beneficial microbes of intestine, improves the health and immunity [19].

Furthermore, presence of medium chain fatty acids (MCFA, C6: C12) content like myristic acid, are better known as an anti-obesity agent, due to its direct absorption to liver, to provide energy [5,18]. Abundance of MUFA including *omega-7* and *omega-9* like oleic acid, vaccenic acid Conjugated Linoleic Acid (CLA) isomer along with traces of fat-soluble vitamins K2, A, D, E contributes to anti-viral, anti-carcinogenic, anti-atherogenic, anti-diabetic, anti-mutagenic, anti-hypertensive, immunomodulatory, apoptotic and osteosynthetic effects [13]. Furthermore, Poly-Unsaturated Fatty Acids (PUFA) mainly include the family of *omega-3* and *omega-6*, like Alpha-linolenic acid (ALA, *omega-3*), and Eicosapentaenoic acid (EPA, *omega-3*) and Docosahexaenoic acid (DHA, *omega-3*) reduces the risk of Cardiovascular Disease (CVD), high cholesterol levels, depression, rheumatoid arthritis and potentially, cancer [8,20].

Presence of the Trans-Fatty Acids (TFA) from ruminants contained in ghee are a consequence of the rTFA have exhibited no negative effect on coronary heart disease risk, as anti-obesity, anti-

carcinogenic, anti-atherogenic, anti-diabetic, anti-mutagenic, anti-hypertensive, immunomodulatory, apoptotic and osteosynthetic [20,21-27].

Why *Ghrita* as Therapeutics?

Ayurved describes at approximately 60 *ghrita* based formulations in detail and has catalogued them in The Ayurvedic pharmacopeia of India, for various diseases and nutraceuticals agent.

Ghritas like *Pachagavya Ghrita*, *Kalayanaka Ghrita*, *Brahmi Ghita* being rich in PUFA i.e., DHA, certain alkaloids and terpenoids are known to improve acetylcholine levels finding its use in CNS disorders, including dementia, schizophrenia, epilepsy, psychosis [2,25,26]. They further are strong antioxidants, so alleviate longevity by free radical movement and are beneficial in age-related heterogeneous group of neurodegenerative diseases affecting the nervous system, brain cells and peripheral nerves. Further in Geriatrics, *Ghritas* simultaneous take care of cardiovascular risk by lowering the LDL attributing to α -Linolenic Acid (ALA) a type of *Omega-3* and rTFA; inflammatory diseases, bone related disorder and work on the immunomodulation [6,22,23].

Ghrita like *Saraswata ghrita* is a well-accepted Pediatric formulation, amounting to triglycerides as per prescribed daily intake for children. These marketed formulations enriched with DHA, are indispensable for children with delayed speech and ADHD (Attention Deficient Hyperactivity Syndrome) [24,28].

Almost all these *ghritas* are having rich phenolic base contributing to all the said uses. Interesting, hydroalcoholic formulations like *Ashwagandharishta* and *Saraswatarishta*, have similar combination of phytoconstituents but when formulated as *Ghritas* are found to be more potent formulations in different sets of health conditions [5,28,29].

Ghritas, the Lipid-based formulation can still be innovatively remodeled to incorporate newer drugs with solubility or permeability challenges. Though, the *Ghritas* find place in the Pharmacopoeias and has large consumer base as nutraceuticals, require commercial exploitation in fields of cosmetics and nasal formulations. Further *Ghritas* have emerging role as phytonutrients-based longevity enhancer.

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