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Review Article

Abundance of Health Benefits from Phytochemicals Using Ayurvedic Herbal Milk-Based Emulsions - Ksheerpak

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Abstract

Milk decoctions and emulsions are an ancient Ayurvedic modality to deliver the goodness of herbs. Milk contains proteins and lipids, which makes it an ideal medium to solubilize both the hydrophobic and hydrophilic phytochemicals present in herbs. The milk proteins and lipids further act like carriers to deliver the bioactives, increasing the stability and bioavailability of the latter. Several classical herbal milk decoctions are mentioned in the Ayurvedic texts, many of which are promotive in action and offer a means to enhance organ and immune functions. The formulatory principle underlying herbal milk emulsions can be utilized to innovate several novel formulations for curing disorders and optimizing systemic functions.

Keywords: Milk Decoctions; Emulsions; ksheerpak, phytochemical carriers; milk proteins

Introduction

Milk decoction (ksheerpak) is a traditional Ayurvedic preparation that involves boiling medicinal herbs in milk to extract their beneficial phytochemical compounds. A large number of phytochemicals are now acknowledged as being healthful. But these have not been able to be freely used because of reasons of bioavailability, since after oral ingestion their absorption is very low. It is being increasingly recognized that many of these phytonutrients need to be in emulsion system to make them more bioavailable [1]. Bioactives like phytosterols, carotenoids and phenolics need an emulsion vehicle to diffuse in the aqueous system of the gut lumen, and cross the lipid membrane of the absorptive intestinal mucosal cells [2,3].

Milk is considered to be an emulsion that suspends oil (milk fats) in the aqueous phase (o/w). Along with fats, milk also contains several types of proteins, which impart added characteristics to the milk emulsion. When used to make a decoction of herbs, the hydrophobic phytochemicals present in the herbs get solubilized in the milk fats, while the hydrophilic ones are solubilized by the water. The milk proteins also act as carriers by binding to several of the bioactives. Thus, most of the phytoactives present in the herbs are brought into solution, as compared to when water or oil alone are used. Also, the milk fats are important for enhancing the absorption of the phytoactives in the small intestines, since the absorptive intestinal cell membranes are composed of lipids. Overall, milk emulsion is an efficient herbal vehicle and a valuable pharmaceutical drug delivery modality.

Emulsions as drug delivery formulations

Emulsions are primarily used for the oral delivery of hydrophobic phytochemicals. The colloidal systems of emulsions can encapsulate a variety of phytochemicals, such as ω-3 fatty acids, carotenoids, curcumin, resveratrol, Coenzyme Q10, and pterostilbene. The phytochemical is typically dissolved in the oil phase before forming the emulsion-based delivery system.

Numerous studies have demonstrated that encapsulating hydrophobic phytochemicals in emulsions or nanoemulsions can increase their bioaccessibility, bioavailability, and bioactivity [4, 5, 6]. For example, *in vivo* studies have shown that encapsulating curcumin within nanoemulsions can increase its oral bioavailability compared to free curcumin. Similarly, the oral bioavailability of β-carotene is significantly higher when delivered as a nanoemulsion rather than dispersed in oil alone [7]. Nanoemulsions also improve the bioaccessibility of phytochemicals such as berberine, lutein and resveratrol [5]. Additionally, nanoemulsions with D-limonene demonstrated improved encapsulation and permeation [8].

The nature of the oil phase used to solubilize the phytochemicals also plays a crucial role in determining their bioaccessibility. For example, carotenoids are more easily solubilized in mixed micelles formed from long-chain triglycerides than those formed from short- or medium-chain triglycerides. As a result, the bioaccessibility of carotenoids is significantly higher in nanoemulsions made from long-chain triglycerides. The emulsifier (milk proteins) coating the lipid droplets may also impact the stability and bioaccessibility of encapsulated phytochemicals within the gastrointestinal tract through various mechanisms, such as retarding or promoting chemical degradation, inhibiting the adsorption of bile salts or lipase to droplet surfaces, and altering the aggregation state of the lipid droplets [5,6,8].

Role of milk proteins in emulsion stabilization

Different milk proteins, including caseins (alpha-casein and beta-casein), whey proteins (beta-lactoglobulin), and lactoferrin, have unique surface-active properties that make them efficient emulsifiers and stabilizers. The amphiphilic caseins and β-Lactoglobulin have a strong tendency to adsorb at the oil/water (O/W) interfaces [9]. The isoelectric point of lactoferrin is 8.5, and this property provides the possibility for preparing O/W emulsions over a wider pH range. Lactoferrin is being widely used in preparation of functional beverages and infant formula. These milk protein-based delivery systems could possibly improve the digestion and absorption of the bioactive phytochemicals like carotenoids within the human gastrointestinal tract.

The quick adsorption of milk proteins to the surface of newly formed oil droplets, when added to oil-water mixtures, leads to a reduction in interfacial tension, allowing for further droplet disruption (Figure 1). The emulsifiers that are better at decreasing the interfacial tension tend to lead to smaller droplets [10], which is advantageous for phytochemical delivery since the bioaccessibility of encapsulated phytochemicals improves as the lipid droplet size decreases.

Figure 1: Milk proteins as phytochemical. carriers and emulsion stabilizers. 1&2- On being added to oil in water emulsions, milk proteins readily adsorb onto the surface of oil droplets, decreasing interfacial tension. 3- When phytochemicals are added to such emulsions, binding takes place between milk proteins and the phytochemicals. 4- If adsorption rate of milk proteins is rapid, there is creation of fine emulsions. 4&5- The milk proteins coating oil droplets prevent flocculation and coalescence, stabilizing the emulsion.

The adsorbed proteins also create a protective membrane around the droplets that resists rupture, stabilizing the droplets against flocculation and coalescence during long-term storage. The protective membrane is formed through the generation of repulsive interactions between the oil droplets, such as steric and electrostatic forces, which prevent them from aggregating. The effectiveness of the milk protein membrane in stabilizing the emulsion thus plays an important role in improving the quality and shelf-life of the emulsion [10].

The role of milk and milk proteins as carriers and versatile emulsifiers for delivering phytochemicals

Milk and milk proteins can play a crucial role in the delivery of hydrophobic nutraceuticals, including phytochemicals. A fine example is that of beta-casein (B-CN) which was studied for its functional capacity as a carrier for curcumin, a natural polyphenol with significant anticancer, anti-inflammatory, and antioxidant properties. The results revealed that B-CN encapsulation increased curcumin solubility by at least 2500-fold, with hydrophobic interactions playing a significant role in the formulation. Encapsulation of curcumin in B-CN micelles also enhanced its antioxidant activity and cytotoxicity against the human leukemia cell line K-562 [11].

Milk proteins and milk protein aggregates have been found to possess various functional properties that facilitate the transportation of hydrophobic nutraceutical substances. Caseins, isolated β-casein, and whey proteins have been investigated for their primary functional transport properties, including binding of molecules or ions, surface activity, aggregation, gelation, and interaction with other polymers. The properties of gelation and interaction with other polymers can be utilized for encapsulating molecules into protein networks. Caseins have been utilized to develop emulsion-based carrier systems due to their surface activity and ability to self-assemble into micelles that can incorporate hydrophobic molecules [12].

A study by Verma *et al* showed that the microfluidized nano-curcumin emulsion using milk cream exhibited improved antioxidant activity and no toxic effects on HepG2 cells, as evidenced by high cell viability. Additionally, bioaccessibility was enhanced by 30%, demonstrating the potential of microfluidization as an effective technique and milk cream as a cost-effective carrier for generating stable and bio-accessible nano-curcumin emulsions [13]. Also, it has been reported that the emulsion of spray-dried curcumin in skim milk exhibited higher encapsulation efficiency and cellular uptake compared to other matrices. The other matrices were a fresh mixture of ethanolic curcumin and skim milk, a powder mixture of curcumin and skim milk powder, and an oil- in -water emulsion [14].

Weng *et al* aimed to create a stable oil-in-water emulsion using bovine milk phospholipid-protein as an emulsifier. The emulsion had a small droplet size and was stable with low concentrations of the milk fatty globule membrane-rich ingredient. The workers also found that the emulsion had a low lipolysis degree during gastric digestion and showed higher hydrolysis efficiency [15].

Yi *et al.*, used milk proteins (whey protein isolate and sodium caseinate) as a stabilizer in the preparation of β-carotene nanoparticles. These whey protein isolate stabilized nanoparticles were found to have the most favorable release properties and improved antioxidant activity compared to free β-carotene. Their study also found that the cellular antioxidant activity of β-carotene was higher when encapsulated in whey protein isolate than in soybean isolate. These findings suggested that whey protein isolate may be the best protein delivery vehicle to deliver β-carotene to the intestine [16]. Another research study on the emulsion-based transport systems for β-carotene found that lactoferrin increased stability of the emulsion over a broad pH range. The study found that lactoferrin along with beta-lactoglobulin, can be engineered to control the function of the interfacial layer, using these mixed protein systems to encapsulate and protect bioactive lipids, such as carotenoids [17]. Manipulation of the interfacial layer is important to engineer the properties and stability of emulsion systems.

Perez studied the potential binding affinity of β-lactoglobulin, a major whey protein in milk, with retinol and fatty acids. His results revealed that β-lactoglobulin could be used as a transporter of small hydrophobic substances, [18]. Another study by Shpigelman explored the potential use of β-lactoglobulin in binding polyphenolic phytochemicals such as EGCG (Epigallocatechin gallate) from green tea. The β-lactoglobulin-EGCG complexes showed good stability and loading efficiency. The study also showed that simulated gastric digestion of β-Lg-EGCG nanoparticles led to a limited release of EGCG, indicating their potential as vehicles for protection and sustained release of EGCG in the intestine [19]. Silva et al. found that milk protein solutions containing different casein-to-whey protein ratios acted as effective emulsifiers, producing stable emulsions with grape seed oil. Milk proteins are also effective in controlling the composition of the interfacial layer, by varying the ratio of caseins to whey proteins in the continuous phase, highlighting the potential of milk proteins as versatile emulsifiers [20].

Furthermore, lactoferrin was studied as an emulsifier for soy oil in emulsions. The study found that the stability of the emulsions decreased as pH approached the protein's isoelectric point. However, stability was restored when β-lactoglobulin or sodium caseinate was added to the serum, indicating the ability of milk proteins to adsorb at the interface and aid in stabilization. The study also suggested other mechanisms beyond electrostatic interactions for emulsion stabilization property of milk proteins [21]. Overall, these studies demonstrate the potential of milk proteins in the delivery and stabilization of bioactive compounds.

Ksheer-Paak: The traditional milk decoction-emulsion

Decoctions made from milk are mentioned in the ancient Ayurvedic texts, and are commonly used. The prescribed milk in Ayurveda is cow's milk, since it is supposed to have special qualities [22].

The preparations are known as ksheer-pak (KP), literally heat-processed milk. Since milk contains significant amounts of lipids, the milk decoctions are in fact, decoction-emulsions. The MILK DECOCTION-EMULSIONS can then be labelled as MDE. The most well known MDE (milk decoction emulsion) is Arjuna (Terminalia arjuna) ksheerpak, a powerful formulation to strengthen the heart. The other Ksheer-paks in common use are those made from Pippali (*Piper longum*) Shatavari (*Asparagus racemosus*) and Ashwagandha (*Withania somnifera*) [23]. Pippali KP is useful in fevers, Ashwagandha KP promotes stamina, and Shatavari KP is useful in pulmonary tuberculosis.

In a study that evaluated the comparative antioxidant activity of milk and water decoctions coriander, ginger, pepper, tulsi, and turmeric using *in vitro* assays, the MDE showed higher antioxidant activity and total phenol content than their water counterparts [24]. This clearly demonstrates the superior effects of milk decoction- emulsions using the same herbs. Of course, to extract maximum benefits from the herbs, the heating process needs to be more prolonged and carried out over low heat. The fundamental principles, for utilizing milk as phytochemical carrier to deliver the pharmacological effects, can be applied to many more formulations for other disease conditions.

Conclusion

Milk and milk proteins have been shown to play a crucial role in delivering hydrophobic nutraceutical substances, such as curcumin, β-carotene, and polyphenolic phytochemicals in an emulsion formulation. Various studies have explored the use of milk proteins and milk protein aggregates as nano vehicles to facilitate the transportation of these substances. Additionally, milk proteins have been used as emulsifiers to create stable oil-in-water emulsions for better delivery of these compounds. Overall, the use of milk, milk protein, and milk emulsion as delivery systems has the potential to improve the solubility, cytotoxicity, antioxidant activity, and release properties of hydrophobic nutraceutical substances, which can have significant implications for the development of functional foods and novel pharmaceutical formulations.

Bibliography

1. Kang J., *et al*. "Non isoflavone Phytochemicals in Soy and their Health Effects". *Journal of Agricultural and Food Chemistry* 58 (2010): 8119-8133.
2. Epriliati I and Ginjom IR. "Bioavailability of Phytochemicals, Phytochemicals - A Global Perspective of Their Role in Nutrition and Health, Dr Venketeshwer Rao (Ed.)". *Intechopen* (2012): 401-428.
3. Kidd P and Head K. "A review of the bioavailability and clinical efficacy of milk thistle phytosome: A silybin-phosphatidylcholine complex (Silipos®)". *Alternative Medicine Review* 10.3 (2005): 193-203.
4. Bali S., *et al*. "Ayurvedic lipid based rasayans - A perspective on the preparation and pharmacological significance of lipids on the bioavailability of phytoconstituents". *Journal of Ayurveda and Integrative Medicine* (2022).
5. McClements DJ. "Advances in nanoparticle and microparticle delivery systems for increasing the dispersibility, stability, and bioactivity of phytochemicals". *Biotechnology Advances* 38 (2020): 107287.
6. Sehgal shubam., *et al*. "Microemulsion: Phytochemical used in new preperations". 5 (2020): 373-376.
7. Fan YT., *et al*. "Development of beta-carotene-loaded organogel-based nanoemulsion with improved *in vitro* and *in vivo* bioaccessibility". *Journal of Agricultural and Food Chemistry* 65.30 (2017): 6188-6194.
8. Mahmood Zaffar., *et al*. "Potential of nano-emulsions as phytochemical delivery system for food preservation". *Pakistan Journal of Pharmaceutical Sciences* 30 (2017): 2259-2263.
9. Liu Y., *et al*. "Effects of milk proteins on release properties and particle morphology of β-carotene emulsions during in vitro digestion". *Food and Function* 5.11 (2014): 2940-2947.

10. Mcclements David. "Protein-stabilized emulsions". *Current Opinion in Colloid and Interface Science* 9 (2004): 305-313.
11. Esmaili M., *et al*. "Beta casein-micelle as a nano vehicle for solubility enhancement of curcumin; food industry application Lebensmittel-wissenschaft + [i.e. Und] Technologie". *Food Science + technology. Science + Technologie Alimentaire* 44.10 (2011): 2166-2172.
12. Kimpel F and Schmitt J J. "Review: Milk Proteins as Nanocarrier Systems for Hydrophobic Nutraceuticals". *Journal of Food Science* 80.11 (2015): R2361-R2366.
13. Verma K., *et al*. "Nanoencapsulated curcumin emulsion utilizing milk cream as a potential vehicle by microfluidization: Bioaccessibility, cytotoxicity and physico-functional properties". *Food Research International* 148 (2021): 110611.
14. Guri A., *et al*. "Delivery of Curcumin Using Skim Milk or Oil in Water Emulsions: Effect of the Matrices on Cellular Uptake". *Journal of Oleo Science* 67.6 (2018): 641-649.
15. Weng J., *et al*. "O/W Emulsion Stabilized by Bovine Milk Phospholipid-Protein Nanoemulsions: Preparation, Stability, and *In Vitro* Digestion". *Journal of Agricultural and Food Chemistry* 69.17 (2021): 5003-5012.
16. Yi J., *et al*. "Beta-carotene encapsulated in food protein nanoparticles reduces peroxyl radical oxidation in Caco-2 cells". *Food Hydrocolloids* 43 (2015): 31-40.
17. Mao Y., *et al*. "Interfacial engineering using mixed protein systems: emulsion-based delivery systems for encapsulation and stabilization of β-carotene". *Journal of Agricultural and Food Chemistry* 61.21 (2013): 5163-5169.
18. Pérez MD and Calvo M. "Interaction of beta-lactoglobulin with retinol and fatty acids and its role as a possible biological function for this protein: a review". *Journal of Dairy Science* 78.5 (1995): 978-988.
19. Shpigelman Avi., *et al*. "Thermally-induced β-lactoglobulin-EGCG nanovehicles: Loading, stability, sensory and digestive-release study". *Food Hydrocolloids* 29 (2012): 57-67.
20. Silva M., *et al*. "Interfacial and emulsification properties of sono-emulsified grape seed oil emulsions stabilized with milk proteins". *Food Chemistry* 309 (2020): 125758.
21. Acero-Lopez A., *et al*. "Characterization of lactoferrin oil-in-water emulsions and their stability in recombined milk". *Journal of Dairy Research* 77.4 (2010): 445-451.
22. Thakare M M and Dobade D K. "Critical Review On Godugdha (Cow Milk) Health Benefits And Hazards". *International Ayurvedic Medical Journal* (2020).
23. Kulkarni M S and Yadav J. "A Review of Kshirpak (Medicated Milk); A Preventive Ayurved Nutraceutical in Various Disease Conditions". *International Journal of Ayurveda and Pharmaceutical Chemistry* 11.1 (2019).
24. Badami S., *et al*. "Antioxidant potential of five Ksheerapaka's and Kashaya's, Ayurvedic decoctions" (2007).