Carrier	Formulation components	Major findings	Reference
Nanoemulsion	β-sitosterol, catechin, polyunsaturated lipid	After emulsified, the melting points and crystallinity of β -sitosterol were reduced	(Wang et al., 2019)
Nanoemulsion	Phytosterol lecithin, monoacyl glycerol, soy lecithin, bulk milk fat	The decreasing in droplet size plays a great impact on lowering crystallization of PS and improving physicochemical stability of emulsion	(Zychowski et al., 2018)
Nanoemulsion	Phytosterol, whey protein, bulk milk fat	Phytosterols at lower concentrations (0.3 wt%) worked together whey protein to reduce effectively interfacial tension.	(Zychowski et al., 2016
Nanoemulsion	Echium oil, phytosterol esters, phenolic compounds, Tween 20	Sinapic acid and rutin showed the highest antioxidant action for phytosterols in emulsion.	(Espinosa et al., 2015)
Microemulsion	Phytosterols, simvastatin sucrose monolaurate, propylene glycol, and oleyl lactate	This microemulsion elevated the dissolution for PSs in the water-free system	(Fisher et al., 2013)
Microemulsion	Ergosterol, Tween 80, Cremophor EL, Cremophor RH40, PEG400, ethanol	In the microemulsions, the water dispersibility of PSs in microemulsions was 1000 times higher than that of free PSs in water and the oral bioavailability of PSs was increased 2.56-fold and 4.5-fold than their unemulsified form.	(Yi et al., 2012)
Microemulsion	β-Sitosterol ester, β- sitosterol, linoleic acid	Beta-sitosterol self-micro emulsion showed a higher lipid-lowering effect than the β- sitosterol powder and tablets.	(Yuan et al., 2019)
Microemulsion	Sitosterol, oryzanol, medium-chain triglycerides, tween 20 Phytosterols, lemon	The emulsions had a good stability and high encapsulation efficiency of more than 80% for 30 days storage period	(Khalid et al., 2017)
Microemulsion	essential oil, polyoxyethylene hydrogenated castor oil, Tween60, polyethylene glycol 400	Microemulsion showed encapsulation efficiency of 89.65% and increased the bioavailability of phytosterols more than three times	(Chuanxun et al., 2019)
oleogel	Phytosterols, oryzanol, sunflower oil	It showed good textural and rheological properties that employed as an alternative of the pig backfat successfully	(Panagiotopoulou et al. 2016)
oleogel	Phytosterols, glycerol monostearate, lecithin, liquid coconut oil	phytosterol-based oleogels containing glycerol monostearate show a substantially higher flow consistency index than that with lecithin did	(Li et al., 2022)
oleogel	β -sitosterol, γ -oryzanol,	chocolate with β -sitosterol/ γ -oryzanol	(Sun et al., 2021)

Table 1 Summary of different delivery carriers for phytosterols

	stearic acid, lecithin, corn oil	oleogel display the strongest gel-forming capacity, the densest gel crystallization	
		network, and similar sensory properties of	
		dark chocolate	
	β-sitosterol, stigmasterol,	Liposomes ergosterol have better capacity in	
Liposome	ergosterol and lanosterol,	maintaining stability in simulated	(Cui et al., 2015)
	lecithin, insulin	gastrointestinal fluid than liposomes	
	Q situational stimulations	prepared with cholesterol	
	β-sitosterol, stigmasterol, campsterol, soybean	The presence of phytosterols affected the	
Liposome	lecithin, ascorbic acid,	liposome stability and encapsulation	(Alexander et al., 2012)
	cholesterol	efficiency of liposome.	
		The stability, encapsulation effectiveness,	
Liposome	β-Sitosterol, lecithin, curcumin	were greatly enhanced with the content of β -	(Tai et al., 2019)
	curcumin	sitosterol was raised from 20 to 33 $\%$	
		Liposome with soy phospholipids, which can	
		encapsulate 35% of PSs. PSs at relatively	
		lower concentration preferentially co-	
Liposome	Phytosterol, phytosterol	assemble into phospholipid bilayers without	(Wang et al., 2017)
	esters, soybean lecithin	the formation of crystals. With the contents	
		of PSs increase at the saturation in system, PSs can be incorporated into the lumen of	
		liposomes and possibly form small crystals.	
	β-sitosterol, green tea	iposonies and possibly form small erystars.	
	extract, grapeseed oil, fish oil, squalene, Tween 20,	The NLCs showed higher antioxidant	
NLC		capacity up to 92% as compared to the free	(Lacatusu et al., 2012)
	Tween 80	β-sitosterol (36.5%).	
		PS-GMS acquired the highest	
	Cmonostearate glycerol,	bioaccessibility due to their sensitivity to the	
SLN	distearate glycerol,	intestinal hydrolysis. An increase in the	(Guo et al., 2022)
	tristearate, lecithin	number of acyl chains of glycerides change	
		their spatial arrangement and inhibits the hydrolysis of ester bonds by enzymes	
		NLC with relatively good physical and	
NLC	β-sitosterol, propolis wax, glyceryl behenate, pomegranate seed oil, Tween 80	chemical stability and ensured the delivery	
		of β -sitosterol to various food Less oil in	(Soleimanian et al.,
		their formulation may result in larger size	2018)
		and lower encapsulation efficiency.	
		NLCs with optimal formulation displayed	
	β-sitosterol, Precirol,	encapsulation efficiency of 99.96%, uniform	
NLC	Miglyol, PEG aqueous	size distribution and increased antioxidant	(Bagherpour et al., 2017)
	phase Poloxamer 407	capacity	G r,2017)
	•	The stability of NLCs in butter preserved no	
		change during the 3-month storage.	

	Phytosterols, fully	The nanoparticles in aqueous dispersion	
NLC	hydrogenated soybean oil,	have lower temperatures for crystallization	
	and soybean oil, soybean	and presented higher thermal resistance.	(da Silva Santos et al.,
	lecithin, ethoxylated		2019)
	sorbitan monooleate		
	β-sitosterol, beeswax,	β-sitosterol loading in NLCs exhibited	
NLC Protein-based nanoparticles	pomegranate seed oil,	increased solubility and gradual release and	(Soleimanian et al.,
	Tween 80 and	reduced total cholesterol and mouse plasma	2020)
	phospholipids	LDL-cholesterol levels	
	FEE	Protein-based nanoparticles exhibited	
	Phytosterol powder, Whey protein concentrate, soy protein isolate and sodium caseinate	smaller particle sizes, higher packaging	(Cao et al., 2016)
		efficiency and loading capacity, better water	
		redispersion and lower crystallinity of PS	
	Stigmasterol, zein and	among them.	_
Protein-based		The nanoparticles were produced with	
nanoparticles	organic solvents	homogenous size, smooth surface, high	(Feng et al., 2019)
•		encapsulation efficiency (97%) and stability	
Carbohydrate-	Phytosterol, Nanoporous	The PS-NSA decrease the crystallinity and	(Ubeyitogullari et al., 2017)
based	starch aerogels (NSA)	improve the water solubility and acquired a	
nanoparticles	supercritical CO2	20-fold higher bioaccessibility than the crude	
nanopurretes	superentiear 002	PSs	
Carbohydrate-	Phytosterol, Nanoporous	Allow preparation of low- and nonfat food	(Ubeyitogullari & Ciftci 2019)
based	starch aerogels (NSA)	enriched with phytosterol and increase their	
nanoparticles	supercritical CO ₂	bioaccessibility from 16 to 53% in non-fat	
nanoparticles	supercritical CO_2	bars	
Complex		Nanoparticles with 5:1 ratio of SPI/pectin	
coacervation of	Phytosterol, soy protein	exhibited higher encapsulation efficiency of	(Feng et al., 2021)
biopolymers	isolate, pectin	87.9% and better stability against gastric	
nanoparticles		acid conditions	
Committee		Gelatin-Arabic gum nanoparticles showed	
Complex	Beta-sitosterol and echium	encapsulation efficiency for α -linolenic,	(Comunian et al., 2018)
coacervation of	seed oil, gelatin, Arabic	stearidonic acid, and β -sitosterol of 96, 90,	
biopolymers			
	gum	and 74%, respectively at 30 days storage	
nanoparticles	gum	and 74%, respectively at 30 days storage period	
nanoparticles Complex	gum	period	
Complex	gum Stigmasterol, zein and	period The loaded stigmasterols in nanoparticles	
Complex coacervation of	Stigmasterol, zein and	period	(Feng et al., 2020)
Complex coacervation of biopolymers	-	period The loaded stigmasterols in nanoparticles	(Feng et al., 2020)
Complex coacervation of biopolymers nanoparticles	Stigmasterol, zein and	period The loaded stigmasterols in nanoparticles can be delivered to the intestine successfully and release 99.07% of them	(Feng et al., 2020)
Complex coacervation of biopolymers nanoparticles Complex	Stigmasterol, zein and pectin	period The loaded stigmasterols in nanoparticles can be delivered to the intestine successfully and release 99.07% of them The SC/pectin-based phytosterols NPs	(Feng et al., 2020)
Complex coacervation of biopolymers nanoparticles Complex coacervation of	Stigmasterol, zein and pectin Phytosterol, sodium	period The loaded stigmasterols in nanoparticles can be delivered to the intestine successfully and release 99.07% of them The SC/pectin-based phytosterols NPs owning high encapsulation efficiency (91%).	(Feng et al., 2020) (Gan et al., 2022)
Complex coacervation of biopolymers nanoparticles Complex coacervation of biopolymers	Stigmasterol, zein and pectin	period The loaded stigmasterols in nanoparticles can be delivered to the intestine successfully and release 99.07% of them The SC/pectin-based phytosterols NPs owning high encapsulation efficiency (91%). The bioaccessibility of PSs was increased by	
Complex coacervation of biopolymers nanoparticles Complex coacervation of	Stigmasterol, zein and pectin Phytosterol, sodium	period The loaded stigmasterols in nanoparticles can be delivered to the intestine successfully and release 99.07% of them The SC/pectin-based phytosterols NPs owning high encapsulation efficiency (91%).	

- Alexander, M., Lopez, A. A., Fang, Y., & Corredig, M. (2012). Incorporation of phytosterols in soy phospholipids nanoliposomes: Encapsulation efficiency and stability. *Lwt*, 47(2), 427-436.
- Bagherpour, S., Alizadeh, A., Ghanbarzadeh, S., Mohammadi, M., & Hamishehkar, H. (2017). Preparation and characterization of Betasitosterol-loaded nanostructured lipid carriers for butter enrichment. *Food bioscience*, 20, 51-55.
- Cao, W.-J., Ou, S.-Y., Lin, W.-F., & Tang, C.-H. (2016). Food protein-based phytosterol nanoparticles: fabrication and characterization. *Food & Function*, 7(9), 3973-3980.
- Chuanxun, Y., Xueru, Z., & Risheng, J. (2019). Development and characterization of phytosterol nanoemulsions and self-microemulsifying drug delivery systems. *bioRxiv*, 585166.
- Comunian, T. A., Nogueira, M., Scolaro, B., Thomazini, M., Ferro-Furtado, R., de Castro, I. A., & Favaro-Trindade, C. S. (2018). Enhancing stability of echium seed oil and beta-sitosterol by their coencapsulation by complex coacervation using different combinations of wall materials and crosslinkers. *Food Chemistry*, 252, 277-284.
- Cui, M., Wu, W., Hovgaard, L., Lu, Y., Chen, D., & Qi, J. (2015). Liposomes containing cholesterol analogues of botanical origin as drug delivery systems to enhance the oral absorption of insulin. *International journal of pharmaceutics*, 489(1-2), 277-284.
- da Silva Santos, V., Miyasaki, E. K., Cardoso, L. P., Ribeiro, A. P. B., & Santana, M. H. A. (2019). Crystallization, polymorphism and stability of nanostructured lipid carriers developed with soybean oil, fully hydrogenated soybean oil and free phytosterols for food applications. *Journal* of Nanotechnology Research, 1(1), 1-21.
- Espinosa, R. R., Inchingolo, R., Alencar, S. M., Rodriguez-Estrada, M. T., & Castro, I. A. (2015). Antioxidant activity of phenolic compounds added to a functional emulsion containing omega-3 fatty acids and plant sterol esters. *Food Chemistry*, 182, 95-104.
- Feng, S., Wang, D., Gan, L., Shao, P., Jiang, L., & Sun, P. (2020). Preparation and characterization of zein/pectin-based phytosterol nanodispersions and kinetic study of phytosterol release during simulated digestion in vitro. *Lwt*, 128, 109446.
- Feng, S., Yan, J., Wang, D., Jiang, L., Sun, P., Xiang, N., & Shao, P. (2021). Preparation and characterization of soybean protein isolate/pectin-based phytosterol nanodispersions and their stability in simulated digestion. *Food Research International*, 143, 110237.
- Feng, S., Zheng, X., Luan, D., Shao, P., & Sun, P. (2019). Preparation and characterization of zein-based phytosterol nanodispersions fabricated by ultrasonic assistant anti-solvent precipitation. *Lwt*, 107, 138-144.
- Fisher, S., Wachtel, E. J., Aserin, A., & Garti, N. (2013). Solubilization of simvastatin and phytosterols in a dilutable microemulsion system. *Colloids and Surfaces B: Biointerfaces*, 107, 35-42. https://doi.org/https://doi.org/10.1016/j.colsurfb.2013.01.036
- Gan, C., Liu, Q., Zhang, Y., Shi, T., He, W.-S., & Jia, C. (2022). A novel phytosterols delivery system based on sodium caseinate-pectin soluble complexes: Improving stability and bioaccessibility. *Food Hydrocolloids*, 124, 107295.
- Guo, S.-J., Ma, C.-G., Hu, Y.-Y., Bai, G., Song, Z.-J., & Cao, X.-Q. (2022). Solid lipid nanoparticles for phytosterols delivery: The acyl chain number of the glyceride matrix affects the arrangement,

stability, and release. Food Chemistry, 133412.

- Khalid, N., Kobayashi, I., Neves, M. A., Uemura, K., Nakajima, M., & Nabetani, H. (2017). Encapsulation of β-sitosterol plus γ-oryzanol in O/W emulsions: Formulation characteristics and stability evaluation with microchannel emulsification. *Food and bioproducts processing*, 102, 222-232.
- Lacatusu, I., Badea, N., Stan, R., & Meghea, A. (2012). Novel bio-active lipid nanocarriers for the stabilization and sustained release of sitosterol. *Nanotechnology*, 23(45), 455702.
- Li, J., Zhai, J., Chang, C., Yang, Y., Drummond, C. J., & Conn, C. E. (2022). Protective effect of surfactant modified phytosterol oleogels on loaded curcumin. J Sci Food Agric. <u>https://doi.org/10.1002/jsfa.12122</u>
- Panagiotopoulou, E., Moschakis, T., & Katsanidis, E. (2016). Sunflower oil organogels and organogelin-water emulsions (part II): Implementation in frankfurter sausages. *Lwt*, 73, 351-356.
- Rudke, A. R., Heleno, S. A., Fernandes, I. P., Prieto, M., Gonçalves, O. H., Rodrigues, A. E., Ferreira, I. C., & Barreiro, M. F. (2019). Microencapsulation of ergosterol and Agaricus bisporus L. extracts by complex coacervation using whey protein and chitosan: Optimization study using response surface methodology. *Lwt*, 103, 228-237.
- Soleimanian, Y., Goli, S. A. H., Varshosaz, J., Di Cesare Mannelli, L., Ghelardini, C., Cirri, M., & Maestrelli, F. (2020). β-Sitosterol Loaded Nanostructured Lipid Carrier: Physical and Oxidative Stability, In Vitro Simulated Digestion and Hypocholesterolemic Activity. *Pharmaceutics*, *12*(4), 386. https://www.mdpi.com/1999-4923/12/4/386
- Soleimanian, Y., Goli, S. A. H., Varshosaz, J., & Maestrelli, F. (2018). Propolis wax nanostructured lipid carrier for delivery of β sitosterol: Effect of formulation variables on physicochemical properties. *Food Chemistry*, *260*, 97-105.
- Sun, P., Xia, B., Ni, Z.-J., Wang, Y., Elam, E., Thakur, K., Ma, Y.-L., & Wei, Z.-J. (2021). Characterization of functional chocolate formulated using oleogels derived from β-sitosterol with γ-oryzanol/lecithin/stearic acid. *Food Chemistry*, 360, 130017.
- Tai, K., Rappolt, M., He, X., Wei, Y., Zhu, S., Zhang, J., Mao, L., Gao, Y., & Yuan, F. (2019). Effect of β-sitosterol on the curcumin-loaded liposomes: Vesicle characteristics, physicochemical stability, in vitro release and bioavailability. *Food Chemistry*, 293, 92-102.
- Ubeyitogullari, A., & Ciftci, O. N. (2019). In vitro bioaccessibility of novel low-crystallinity phytosterol nanoparticles in non-fat and regular-fat foods. *Food Research International*, *123*, 27-35.
- Ubeyitogullari, A., Moreau, R., Rose, D. J., Zhang, J., & Ciftci, O. N. (2017). Enhancing the bioaccessibility of phytosterols using nanoporous corn and wheat starch bioaerogels. *European Journal of Lipid Science and Technology*, 121(1), 1700229.
- Wang, F. C., Acevedo, N., & Marangoni, A. G. (2017). Encapsulation of phytosterols and phytosterol esters in liposomes made with soy phospholipids by high pressure homogenization. *Food Funct*, 8(11), 3964-3969. <u>https://doi.org/10.1039/c7fo00905d</u>
- Wang, X., Li, X., Xu, D., Zhu, Y., Cao, Y., Wang, J., & Sun, B. (2019). Comparision of heteroaggregation, layer-by-layer and directly mixing techniques on the physical properties and in vitro digestion of emulsions. *Food Hydrocolloids*, 95, 228-237.
- Yi, C., Zhong, H., Tong, S., Cao, X., Firempong, C. K., Liu, H., Fu, M., Yang, Y., Feng, Y., & Zhang, H. (2012). Enhanced oral bioavailability of a sterol-loaded microemulsion formulation of Flammulina velutipes, a potential antitumor drug. *International journal of nanomedicine*, 7, 5067.

- Yuan, C., Zhang, X., Long, X., Jin, J., & Jin, R. (2019). Effect of beta-sitosterol self-microemulsion and beta-sitosterol ester with linoleic acid on lipid-lowering in hyperlipidemic mice. *Lipids Health Dis*, 18(1), 157. <u>https://doi.org/10.1186/s12944-019-1096-2</u>
- Zychowski, L. M., Logan, A., Augustin, M. A., Kelly, A. L., O'Mahony, J. A., Conn, C. E., & Auty, M. A. E. (2018). Phytosterol crystallisation within bulk and dispersed triacylglycerol matrices as influenced by oil droplet size and low molecular weight surfactant addition. *Food Chem*, 264, 24-33. <u>https://doi.org/10.1016/j.foodchem.2018.04.026</u>
- Zychowski, L. M., Logan, A., Augustin, M. A., Kelly, A. L., Zabara, A., O'Mahony, J. A., Conn, C. E., & Auty, M. A. (2016). Effect of phytosterols on the crystallization behavior of oil-in-water milk fat emulsions. *Journal of Agricultural and Food Chemistry*, 64(34), 6546-6554.