Citrus flavonoids (naringin and hesperidin) as functional ingredients in dairy products

Chandimala UR[1,2*], *Zsolt* Ajtony[1], and *Beatrix* Sik[1]

[1]Department of Food Science, Albert Kázmér Faculty of Agricultural and Food Sciences, Széchenyi István University, Mosonmagyaróvár, Hungary
[2] Department of Food Technology, Institute for Agro-Technology and Rural Sciences, University of Colombo, Hambantota, Sri Lanka

Abstract. Recently, the development of functional foods enriched with plant phenolic compounds attracted the attention of researchers due to their favorable health properties. Naringin (NAR) and hesperidin (HES) are two main bioflavonoids available in high concentrations in citrus (CTS) fruits, including juice processing by-products like peel, membranes, and seeds. In general, NAR and HES offer potential health benefits in various diseases including diabetes mellitus, certain types of cancer, and obesity. However, to take advantage of the benefits of flavonoids in CTS, researchers must consider various factors since the development of enriched food is valueless if the bioactive compounds are not stable in the food matrix or are not absorbed appropriately throughout the digestive system. This study presents the sensory, physicochemical, and organoleptic properties of CTS-enriched dairy products produced by different technologies. This paper also includes the extraction methods, encapsulation technologies, and beneficial effects of NAR and HES. Overall, results supported that incorporating HES and NAR improves the antioxidant properties and, in some cases, the consumer acceptance of dairy products. In the future, the application of encapsulation technologies will probably come to the fore in the functional food industry, since encapsulation is used to mask unpleasant feelings during eating, such as the bitter taste of CTS flavonoids.

1 Introduction

Citrus (CTS) crops belong to the family of the Rutaceae and Aurantioidae subfamily. Among the citrus species, sweet orange (*Citrus sinensis*), lemon (*C. limon*), lime (*C. aurantifolia*), grapefruit (*C. paradisi*), pomelo (*C. grandis*), mandarin (*C. reticulata*), and tangerine (*C. reticulata deliciosa*) are known as the most commercially important. In recent years, various studies have shown that CTS flavonoids have many beneficial effects on human health, including improving blood lipid profiles and reducing blood pressure, stroke, cardiovascular disease (CVD), cancer threat, and obesity [1]. The consumption of fresh CTS fruits and their products (e.g., juices, fruit concentrates, nectar, and marmalades) has increased remarkably in recent years. CTS is the second most produced fruit in the world, with a global production of 161.8 million tons in 2021, and China, Brazil, and India are the top three producers. From

*Corresponding author: rushanthi@uciars.cmb.ac.lk

2011 to 2021, there has been a notable increase (73-162 million tons) in the production of CTS fruits [2]. The increase in the production and consumption of CTS fruits has resulted in a trend of novel research studies on CTS polyphenols [2]. CTS fruits are good sources of phenolic compounds, especially flavonoids (flavones, flavanones, and flavonols). It is well-known that flavanones affect significantly the organoleptic properties of CTS fruits. The bitter taste of CTS is due to compounds such as NAR, limonin, and poncirin. Therefore, their use as functional food ingredients is challenging. The encapsulation (ENC) process is a good solution for masking unpleasant tastes of CTS fruits. The methodology is based on entrapping phenolic compounds within a wall material [3]. In addition, ENC may also improve the water solubility, physicochemical stability, and absorption capacity of encapsulated polyphenols in the gut [4]. To protect CTS flavonoids and release them in a controlled manner within the product, nanoparticles, microspheres, or coatings can be formed. Although different ENC methods have been suggested, none of them can be recognized as entirely applicable for delivering polyphenols in dairy foods because the molecular structure of each polyphenol has an impact on the effectiveness of delivery via each technology [5].

Recent studies have shown that dairy products are a good matrix for delivering phenolic compounds to the body. Currently, several studies have been published where CTS peel extracts were incorporated into various foods, including kefir, paneer, yogurt, and cheese. [6, 7]. However, it is also well-known that polyphenols may interact with globular proteins in milk thus reducing the antioxidant activity (AA) and bioavailability of these functional components [5]. Other physicochemical properties of CTS flavonoids, such as poor water solubility, poor dissolution rate, and susceptibility to oxidation, also limit their use in free form in dairy products and other beverages [8, 9]. According to the databases, studies and critical reviews focusing on the ENC of naringin (NAR) and hesperidin (HES) in CTS fruits for use in functional foods are very limited even though they are highly prevalent in CTS fruits, particularly in peel. This review describes the extraction methods of HES and NAR from CTS fruits and ENC technologies applied to use them in functional dairy food products.

2 NAR and HES in CTS fruits

From a chemical point of view, NAR ($C_{27}H_{32}O_{14}$) and HES ($C_{28}H_{34}O_{15}$) are polar flavanone glycosides [10]. Chemically, HES has an aglycon, namely hesperetin or methyl eriodyctiol bonded to disaccharides such as rutinose [11]. Previous HPLC measurements revealed that flavanone glycosides exist as diastereomers due to a chiral center in the C-2 position of the flavanone moiety and the diastereomeric flavanone glycosides differ in their physicochemical properties [12]. The chemical structure of HES is similar to NAR's, except that HES has an additional methoxy (O–CH_3) group [13]. Both flavanone glycosides are poorly soluble in water (HES: 4.95 μg/mL; NAR: 500-1000 μg/mL while more soluble in organic solvents such as methanol and ethanol. HES is an odorless and tasteless light-yellowish crystalline powder with a melting point of 258 ˚C-262 ˚C [4,8,11]. NAR is a white to yellow powder with a melting point of 166˚-170˚C [4, 8].

NAR is accountable for the bitter taste of fruits such as grapefruit and pummelo, commonly found in the peel, seeds, and flesh of CTS fruits and its amount is higher in immature fruits [14]. Recent studies have proven that CTS fruit peel is richer in NAR than the pulp [13]. Flavedo, albedo, pith, and membranes contain higher HES levels than juice vesicles and seeds of CTS fruits [9]. NAR is the most dominant flavanone glycoside compound (>92%) in grapefruit whereas HES is dominant in the lemon, Liucheng, Ponkan, and Tonkan peel extracts [1, 13].

3 Bioavailability and health benefits of CTS flavonoids

3.1 Bioavailability of HES and NAR

NAR is enzymatically metabolized in the stomach by β-glycosidase and further broken down to naringenin in the human gut by enzymes of the intestinal microflora during digestion. HES cannot be absorbed by the intestinal wall. During digestion in the colon, HES is converted into hesperitin by the intestinal microflora, and after glucuronidation to hesperitin glucuronide, it is absorbed into the plasma [11]. Applications of NAR and HES in the food industry are restricted because of their low solubility and stability [4,8,13].

3.2 Antioxidant and anti-inflammatory properties of NAR and HES

NAR has been found to possess antioxidant potential owing to its excellent radical scavenging ability [4, 8]. HES shows AA in two ways; by direct radical scavenging [9] and the antioxidant cellular defenses via the ERK/Nrf2 signaling pathway [15]. Also, HES has the potential to inhibit the formation of advanced glycation end-products which can cause random damage in extracellular proteins [15]. The anti-inflammatory activities of HES are known to be caused by the attenuation of over-active macrophages and the amplification of the function of dysfunctional T lymphocytes [15]. Oxidative stress and inflammations are associated with most non-communicable diseases such as CVD, cancers, and neurodegenerative diseases [15]. NAR has shown anti-diabetic, and anti-cancer activities in addition to its protective effects against CVD, and hence, NAR supplementation is used to treat several degenerative diseases [4, 8]. Being able to induce apoptosis, HES is being studied extensively in treating several cancers [14]. HES can heal the DNA damage caused by UV irradiation and demonstrates diuretic, hypolipidemic, and antihypertensive functions. It is also known to reduce capillary permeability [7, 14].

3.3 Antibacterial properties of NAR and HES

NAR and HES in grapefruit seed and pulp extracts have shown effective inhibitory effects on Gram-positive and Gram-negative bacteria in a broth susceptibility test [16]. This can be explained by several mechanisms such as interference with DNA synthesis, bacterial enzymes, membrane permeability, and activation of host defense. However, the antibacterial activity of CTS flavonoids may vary with the effect of some other factors such as molecular structure, solubility, presence of sugar moiety, and the type of sugar moiety [16].

4 Isolation of CTS flavonoids

The extraction of CTS flavonoids is challenging because of their chemical complexity. Moreover, the effectiveness of extraction depends on several factors, including, the type of solvent used, extraction time, temperature, and liquid-solid ratio [17]. Therefore, in addition to optimizing the extraction parameters, selecting the appropriate extraction method is crucial. Conventional extraction methods such as Soxhlet extraction (SXE) or heat reflux extraction (HRE) are commonly used to extract CTS flavonoids. However, these methods have several drawbacks; excess time and solvent consumption, difficulty in automation, and high solvent consumption [18]. For this reason, in recent years, researchers have preferred non-conventional methods due to their favorable properties. High-pressure extraction (HPE) attracted the attention of researchers due to its energy efficiency. Overall, it uses high pressure (100-1000 MPa) which may allow extract higher bioactive compound yields in a short time. Compared to conventional methods, HPE admits higher-quality extracts since it operates at lower temperatures and with less solvent [19]. For large-scale commercial extractions, ultrasonic-assisted extraction (USAE) is considered an efficient technique.

Similar to HPE, the application of USAE in flavonoid recovery may cause a higher extraction yield with a shorter extraction time [20]. Although USAE combined with deep eutectic solvents (DES) seems a promising method for HES extraction due to its efficiency (65%), it should be noted that the recovery of flavonoids from DES is challenging [21].

Sub/supercritical water extraction (SWE) is also a promising method since it is economically safe and provides higher selectivity. This method usually uses supercritical carbon dioxide (CO_2). At the same time, it is also important to note that the use of unmodified CO_2 may reduce the selectivity of the method. To avoid this drawback, researchers use solvent modifiers such as methanol, ethanol, and acetonitrile [20]. Cheig *et al.* [22] isolated 73 mg/g HES from CTS peel with a 100% recovery rate. Overall, this yield was 1.9, 3.2, and 34.2-fold higher than conventional 70% ethanol, 70% methanol, and hot water (90˚C) extraction. Microwave-assisted extraction (MAE) is based on microwave energy absorption by polar molecules. The main advantage of this technique is that microwave radiation enhances the evaporation of residual water from plant materials and breaks their cell walls. Generally, MAE provides better extraction efficiency within a shorter period than the Soxhlet method, HRE, and SWE [20, 23]. Inoue *et al.* [24] extracted HES from *Citrus unshiu* peel waste by MAE. Extraction was performed in a closed system at 60-180˚C for 7 min using 70% ethanol. Under this condition, the extractable HES concentration was 58.6 mg/g.

As mentioned above conventional methods are often used for CTS fruit extraction due to their simplicity. SXE is one of the most commonly applied conventional methods to extract phenolic compounds [18]. However, its efficiency is significantly lower than MAE. Iglesias-Carres *et al.* [17] reported an extractable HES concentration of 20 mg/g using SXE. For NAR, Yusof *et al.* [14] presented an extractable concentration of 29-3910 μg/g by SXE, using methanol as solvent. HRE is also considered a conventional method that involves heating the plant material in a solvent up to high temperatures (70-80˚C) which takes a shorter time than the SXE [23].

After extraction, researchers usually use chromatographic methods to determine single CTS flavonoids. Ni *et al.* [25] developed an HPLC procedure combining HPLC and solid-phase extraction to quantify NAR in citrus juice. This method demonstrated a retention time of 14.7 min and 92.2-100.6% recovery value for NAR. Chen *et al.* [26] first established a novel, HPLC-UV method to analyze simultaneously four CTS flavonoids. The method was successfully applied to the identification of HES, neohesperidin, neohesperidin dihydrochalcone, and hesperetin from *Fructus aurantii immaturus* and *Pericarpium citri reticulatae* extracts. HES recovery was high with a value of 92.7%.

5 ENC methods of NAR and HES

Table 1 shows different ENC methods have been applied and studied in previous research. The ENC can mask the bitter taste and improve the solubility, stability, and bioaccessibility of NAR, and HES. Nevertheless, the ENC efficiency of these polyphenols as pure compounds and CTS extracts may differ due to the effects of other compounds in the extracts [8, 27]. The first reported literature on microencapsulation (M_{ENC}) of NAR using a food-grade carrier material revealed that cyclodextrin complexation can improve the dissolution rate of CTS flavonoids [28, 29]. Recently, pH-driven methods have become extremely attractive due to their cost- and energy-saving during operation [30, 31]. The principle used in this method is that water-soluble polyphenols are deprotonated at alkaline pH conditions and when the pH becomes acidic, they are driven from the aqueous media into the hydrophobic region [31]. Nanoencapsulation (N_{ENC}) of bioactive compounds is widely studied in many novel research studies mainly due to its high constancy, bioavailability, and good permeability. [32, 33].

Table 1. ENC Methods of NAR and HES.

ENC method	Carrier material	Main Result	Ref.
NAR			
M_{ENC}	β-cyclodextrin	Cyclodextrin complexation could increase the solubility of NAR in water at 37˚C by 15 times than that of free NAR (1.9 μg/mL) and the rate of enzymatic hydrolysis of NAR into naringenin.	[29]
pH-driven ENC (pH shift from 12 to 6)	Lecithin	Nanoliposomes loaded with NAR showed an ENC efficiency of 46–65% with a 6-8% NAR loading capacity.	[8]
N_{ENC}	Gold particles stabilized with gum tragacanth	The best stability of this system was in the pH range of 3-8. Also, a 76% NAR loading capacity could be achieved.	[33]
HES			
Spray-drying and freeze-drying ENC	Maltodextrin and gum arabic	The freeze-drying procedure was more suitable for pure HES ENC whereas spray drying showed remarkable results for HES in CTS peel extract. Maltodextrin was better for HES both in pure form and CTS peel extract. Gum arabic was better in freeze-drying pure HES.	[27]
Oil-in-water emulsion	Chitosan in water and HES in refined soybean oil	ENC efficiency was above 70% at 20˚C and 40˚C after 30 days of storage	[34]
Extrusion/external gelation	Alginate microparticles coated with polyelectrolytes (chitosan and gelatin or synthetic polymers)	The ENC efficiency was higher than 98% in MPs composed only of biopolymers while that of MPs with synthetic polymers was 87.9%. MPs produced by combining chitosan, gelatin, and alginate provided the best protection for HES against gastric conditions and controlled release	[3]

6 Dairy product enrichment incorporating CTS flavonoids

Previous studies have shown that CTS fruits may be used as a potential natural preservative in dairy products due to their antioxidant and antimicrobial properties. More specifically, AA of CTS flavonoids was known to suppress lipid oxidation in dairy products [35]. For instance, Afshari and Fadaei [35] showed that a reduction of acidity and an increase in the AA and dry matter content leading to an increase in the product's viscosity can be observed in milk when enriched with bitter orange peel extract. At the same time, the enrichment step may significantly affect the consumer acceptance and functional and textural properties of dairy products, especially if the CTS fruits are added in free form to products. For instance, Acharjee *et al*. [36] showed that the firmness of yogurt enriched with orange pomace powder decreased during storage. Although the ENC step of CTS flavonoids may provide additional health benefits, improve product stability, and enhance flavor and texture attributes, the available research is very limited. Table 2 shows a summary of existing literature about the enrichment of dairy products incorporating CTS flavonoids.

Table 2. Enrichment of Dairy Products with CTS Flavonoids.

Plant extract	Applied form	Used concentration	Food product	Main results	Ref.
Lemon and orange	Peel extract	1-3%	Paneer	Decreased peroxide value in comparison to control. Good overall acceptability up to 1-2% use of antioxidant extracts.	[6]
Orange, mandarin, and lemon	Pomace powder	1%, 3%, 5%	Yogurt	The best biological activities were present in 5% orange pomace yogurt. The pH values of all samples decreased, while acidity, fat, and total soluble solids increased. The 1 and 3% orange pomace yogurts scored higher in color, flavor, and structure than other samples.	[37]
Sour orange, sweet orange, and lemon	Peel extract	0.5%	Yogurt	CTS peels did not affect the overall acceptability of symbiotic yogurt. Increased acidity and decreased moisture properties during cold storage. Improved antioxidant and antibacterial activities.	[38]
Bitter orange and lemon	Peel extract	10 (orange) and 17(lemon) mL/100g of dairy product	Kefir	Estimated total antioxidant bioavailability index (*in vitro* digestion model); bitter orange: 42%, lemon: 36%. Higher antioxidant properties. Similar overall acceptability as the control sample.	[7]
Orange	Encapsulated peel extract	Respective ratio of encapsulated peel extract to obtain 300, 600, and 900 mg phenolic content	Yogurt	Supplementation had no significant impact on the texture and physicochemical properties of yogurt up to 900 mg of phenolic content. Organoleptic properties were acceptable.	[39]

Although the enrichment with CTS fruit extracts may increase the AA, antimicrobial effects and organoleptic quality of certain dairy products, there are some crucial and challenging factors to be considered. First, the organic solvent used for the extraction of CTS flavonoid should be of food grade, or else, toxicological tests must be conducted for the food product [40]. Similarly, food-grade carrier materials should be used for the ENC of CTS flavonoids. Second, the novel CTS flavonoid-enriched dairy product should be compared with existing commercial products for their acceptability [40]. In addition to that, testing the bioavailability of CTS flavonoids in enriched dairy products after *in-vitro* digestion is crucial. In summary, we summarize that safety, nutritional, sensory and commercial aspects must be considered regarding the enrichment of dairy products with CTS flavonoids.

7 Conclusion

With the increased production of CTS fruits, the accumulation of by-products of CTS juice processing has increased. HES and NAR have a variety of therapeutic and medical effects on the human body. For the extraction of CTS flavonoids, novel methods such as MAE, SWE, HPE, and USAE are promising due to their capacity to give better extraction yields with higher extraction efficiency at shorter times. This review concludes that the incorporation of CTS flavonoids into dairy products can improve the antimicrobial and antioxidant potential of those products. Nevertheless, incorporating CTS flavonoids into dairy products is challenging due to their low solubility, bioavailability, unknown chemical reactions, and stability. ENC is an effective technology to deliver nutraceuticals to consumers through food products by improving their stability and bioavailability without harming the product's sensory attributes. Overall, this review provides insight into the existing ENC technologies for CTS flavonoids, and the potential to incorporate them into dairy products opening up a new arena in the functional food industry to be further investigated. Optimization of the ideal ENC method for NAR and HES depending on the type of dairy product and studying their functioning in the human body based on *in vitro* studies is crucial to generate better results.

References

1. Y. S. Huang, S. C. Ho, Polymethoxy flavones are responsible for the anti-inflammatory activity of citrus fruit peel. Food Chem. **119**(3), 868-873 (2010). https://doi.org/10.1016/j.foodchem.2009.09.092
2. M. K. Khan, Z. E. Huma, O. Dangles, A comprehensive review on flavanones, the major citrus polyphenols. J. Food Compos. Anal. **33**, 85-104 (2014). https://doi.org/10.1016/j.jfca.2013.11.004
3. M.T. Maniecka, L. Lamch, I. Chojnacka, R. Gancarz, K.A. Wilk, Microencapsulation of Hesperidin in polyelectrolyte complex microbeads: Physico-chemical evaluation and release behavior. J. Food Eng. **214**, 104-216 (2017). https://doi.org/10.1016/j.jfoodeng.2017.06.015
4. J. Zhang, P. Zhang, T. Liu, T. Zhou, L. Zhang, R. Lin, G. Yang, W. Wang, Y. Li, Solubility of Naringin in ethanol and water mixtures from 283.15 to 318.15K. J. Mol. Liq. **203**, 98-103 (2015). https://doi.org/10.1016/j.molliq.2014.12.039
5. F. Adinepour, S. Pouramin, A. Rashidinejad, S. M. Jafari, Fortification/enrichment of milk and dairy products by encapsulated bioactive ingredients. Food Res Int. **157** (2022). https://doi.org/10.1016/j.foodres.2022.111212
6. S. Singh, G. Immanuel, Extraction of antioxidants from fruit peels and its utilization in paneer. J Food Process Techno. **5**, 349-353 (2014). http://dx.doi.org/10.4172/2157-7110.1000349
7. Kandyliari, P. Potsaki, P. Bousdouni, C. Kaloteraki, M. Christofilea, K. Almpounioti, A. Moutsou, C.K. Fasoulis, L.V. Polychronis, V.K. Gkalpinos. Development of dairy products fortified with plant extracts: antioxidant and phenolic content characterization. Antioxidants. **12** (2023). https://doi.org/10.3390/antiox12020500
8. M. Chen, R. Li, Y. Gao, Y. Zheng, L. Liao, Y. Cao, J. Li, W. Zhou, Encapsulation of hydrophobic and low-soluble polyphenols into nanoliposomes by Ph-driven method: naringenin and naringin as model compounds. Foods. **10**(923) (2021). https://doi.org/10.3390/foods10050963
9. M. F. Rehman, A. I. Batool, R. Qadir, M. Aslam, Hesperidin and naringenin. A Centum of Valuable Plant Bioactives (Elsevier Academic Press 2021).

10. Y. He, Z. Sun, J.Y. Bai, Y. Zhang, Y. Qian, X. Zhao, S. Chen, Citrus peel polyphenols alleviate intestinal inflammation in mice with dextran sulfate sodium-induced acute colitis. Helion. **9**, (2023). https://doi.org/10.1016/j.heliyon.2023.e18137
11. S.D. Ray, M. Krmic, A. Hussain, C. Marvilli, R. Fabian, A. Niha, M. Danai, Z. Smith, A. Jalshgari, N. Malik, A. Alhariri, R. Maldonado, Encyclopedia of Toxicology. (Elsevier Academic Press, 2024).
12. N. Uchiyama, I.H. Kim, N. Kawahara, Y. Goda, HPLC separation of hesperidin and the C-2 epimer in commercial hesperidin samples and herbal medicines. Chirality. **17**, 373-377 (2005). https://doi.org/10.1002/chir.20175
13. V. Altunayar-Unsalan, O. Unsalan, T. Mavromoustakos, Insights into molecular mechanism of action of citrus flavonoids Hesperidin and Naringin on lipid bilayers using spectroscopic, calorimetric, microscopic and theoretical studies. J. Mol. Liq. **347**. (2022). https://doi.org/10.1016/j.molliq.2021.118411
14. S. Yusof, H. M. Ghazali, G. S. King, Naringin content in local citrus fruits. Food Chem. **37**, 113-121. (1990). https://doi.org/10.1016/0308-8146(90)90085-I
15. H. Parhiz, A. Roohbakhsh, F. Soltani, R. Rezaee, M. Iranshahi, Antioxidant and anti-inflammatory properties of the citrus flavonoids hesperidin and hesperetin: an updated review of their molecular mechanisms and experimental models. Phytother Res. **29**. (2015). https://doi.org/10.1002/ptr.5256
16. M. Iranshahi, R. Rezaee, H. Parhiz, A. Roohbakhsh, F. Soltani, Protective effects of flavonoids against microbes and toxins: The cases of hesperidin and hesperetin. Life Sci. **137**. (2015). 125-132. https://doi.org/10.1016/j.lfs.2015.07.014
17. L. Iglesias-Carres, A. Mas-Capdevila, F.I. Bravo, G. Aragonès, B. Muguerza, A. Arola-Arnal. Optimization of a polyphenol extraction method for sweet orange pulp (Citrus sinensis L.) to identify phenolic compounds consumed from sweet oranges. PLoS ONE. **14**(1). (2019). https://doi.org/10.1371/journal.pone.0211267
18. M. Pirzada, Z. Altintas, Molecular Imprinting for Nanosensors and Other Sensing Applications. (Elsevier 2021).
19. S.A. Khan, R. Aslam, H.A. Makroo, High-pressure extraction and its application in the extraction of bio-active compounds: A review. J. Food Process Eng. **42**(1). (2018). http://dx.doi.org/10.1111/jfpe.12896
20. S.N.H.M. Azmin, Z.A. Manan, S.R.W. Alwi, L.S. Chua, A.A. Mustaffa, N.A. Yunus. Herbal processing and extraction technologies. Sep. Purif. Rev. **45**(4), 305-320. (2016). http://dx.doi.org/10.1080/15422119.2016.1145395
21. M. Xu, L. Ran, N. Chen, X. Fan, D. Ren. Polarity-dependent extraction of flavonoids from citrus peel waste using a tailor-made deep eutectic solvent. Food Chem. **297**. (2019). https://doi.org/10.1016/j.foodchem.2019.124970
22. C.I. Cheigh, E.Y. Chung, M.S. Chung, Enhanced extraction of flavanones hesperidin and narirutin from citrus unshiu peel using subcritical water, J. Food Eng. **110**(3), 472-477. (2012). https://doi.org/10.1016/j.jfoodeng.2011.12.019
23. X. Pan, G. Niu, H. Liu, Comparison of microwave-assisted extraction and conventional extraction techniques for the extraction of tanshinones from Salvia miltiorrhiza bunge. Biochem. Eng. J. **12**(1), 71-77. (2002). https://doi.org/10.1016/S1369-703X(02)00039-6
24. T. Inoue, S. Tsubaki, K. Ogawa, K. Onishi, J.I. Azuma, Isolation of hesperidin from peels of Citrus unshi fruits by microwave-assisted extraction. Food Chem. **123**, 542–547. (2010). http://dx.doi.org/10.1016/j.foodchem.2010.04.051

25. H. Ni, S.F. Zhang, Q.F. Gao, H. Yang, Z.D., Jiang, F. Cheng. Development and evaluation of simultaneous quantification of naringin, prunin, naringenin, and limonin in citrus juice, Food Sci Biotechnol. **24**, 1239–1247. (2015). https://doi.org/10.1007/s10068-015-0159-z
26. L. Chen, S. Zhu, C. Wang, L. Chen Development of a HPLC-UV method for the separation and quantification of hesperidin, neohesperidin, neohesperidin dihydrochalcone and hesperetin, Nat. Prod. Res. **37**(10), 1714-1718. (2023). doi=10.1080/14786419.2022.2104275
27. M. Banožić, M. Krzywonos, K. Aladić, H. Pińkowska, I. Mucha, A. Złocińska, S. Jokić, Physicochemical, structural characterization and evaluation of encapsulated Hesperidin from natural sources: Comparison of two encapsulation techniques; spray drying and freeze drying. J. Drug Deliv. Technol. **90**. (2023). https://doi.org/10.1016/j.jddst.2023.105098
28. R. Ficarra, S. Tommasini, D. Raneri, M.L. Calabrò, M.R. Di Bella, C. Rustichelli, M.C. Gamberini, P. Ficarra, Study of flavonoids/β-cyclodextrins inclusion complexes by NMR, FT-IR, DSC, X-ray investigation. JPBS. **29**(6), 1005-1014. (2002). https://doi.org/10.1016/s0731-7085(02)00141-3
29. L. Cui, Z. H. Zhang, E. Sun, X. B. Jia, Effect of β-cyclodextrin complexation on solubility and enzymatic conversion of Naringin. Int. J. Mol. Sci. **13**(11), 14251-14261. (2012). https://doi.org/10.3390/ijms131114251
30. P. Sengupta, D. Das, S. Bhattacharya, R. Sur, A. Bose, K. Sen, A pH-driven method for liposomal encapsulation of dietary flavonoid rutin: Sustained release and enhanced bioefficacy. Food Biosci. **52**. (2023). http://dx.doi.org/10.1016/j.fbio.2023.102392
31. A. Csuti, B. Zheng, H. Zhou, Post pH-driven encapsulation of polyphenols in next-generation foods: principles, formation and applications. Crit. Rev. Food Sci. Nutr. **18**, 1-15. (2023). https://doi.org/10.1080/10408398.2023.2258214
32. W. Tang, Y. Wei, W. Lu, D. Chen, Q. Ye, C. Zhang, Y. Chen, C. Xiao, Fabrication, characterization of carboxymethyl konjac glucomannan/ovalbumin- Naringin nanoparticles with improving in vitro bioaccessibility. Food Chem. **16**. (2022). https://doi.org/10.1016/j.fochx.2022.100477
33. K. Rao, M. Imran, T. Jabri, I. Ali, S. Perveen, A. S. Shafiullah, M. R. Shah, Gum tragacanth stabilized green gold nanoparticles as cargos for Naringin loading: A morphological investigation through AFM. Carbohydr. Polym. **174**, 243-252. (2017). https://doi.org/10.1016/j.carbpol.2017.06.071
34. I. Dammak, P.J.D.A. Sobral, Effect of different biopolymers on the stability of Hesperidin-encapsulating O/W emulsions, J. Food Eng. **237**, 33-43. (2018). https://doi.org/10.1016/j.jfoodeng.2018.05.004
35. A. J. Afshari, V. Fadaei, Characterization of flavored milk containing bitter orange peel extract and Gaz-angubin. Food Sci Nutr. **9**, 164–171 (2021). https://doi.org/10.1002/fsn3.1975
36. A. Acharjee, S.M. Afrin, N. Sit, Physicochemical, textural, and rheological properties of yoghurt enriched with orange pomace powder. J. Food Process Preser. **45**, (2021). https://doi.org/10.1111/jfpp.15193
37. S. A. Alamoudi, A. M. Saad, N. H. Alsubhi, G. I. Alrefaei, D. A. Al-Quwaie, N. Binothman, M. Aljadani, M. Alharbi, H. Alanazi, A. O. Babalghith, M. S. Almuhayawi, H. S. Gattan, M. H. Alruhaili, S. Selim, Upgrading the physiochemical and sensory quality of yogurt by incorporating polyphenol-enriched citrus pomaces

with antioxidant, antimicrobial, and antitumor activities. Front. Nutr. **9**. (2022). https://doi.org/10.3389/fnut.2022.999581

38. H. M. Fathy, A. A. Abd El-Maksoud, W. Cheng, F. M. F. Elshaghabee, Value-added utilization of citrus peels in improving functional properties and probiotic viability of *acidophilus-bifidus-thermophilus* (abt)-type synbiotic yoghurt during cold storage. Foods. **11**(17). (2022). https://doi.org/10.3390/foods11172677
39. T. M. El-Messery, M. M. El-Said, N. M. Shahein, H. M. F. El-Din, A. Farrag, Functional yoghurt supplemented with extract orange peel encapsulated using coacervation technique. PJBS. **22**, 231-238. (2019). https://doi.org/10.3923/pjbs.2019.231.238
40. D. Granato, J.S. Santos, R.D.S. Salem, A.M. Mortazavian, R.S. Rocha, A.G. Cruz, Effects of herbal extracts on quality traits of yogurts, cheeses, fermented milks, and ice creams: a technological perspective. Curr. Opin. Food Sci. 19, 1-7. (2018). https://doi.org/10.1016/j.cofs.2017.11.013