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Nanoemulsion delivery system of tea polyphenols enhanced the bioavailability of catechins in rats

Yunru Peng[a,1], Qilu Meng[a,1], Jie Zhou[a], Bo Chen[a], Junjun Xi[a], Piaopiao Long[a], Liang Zhang[a,b,*], Ruyan Hou[a,b,*]

[a] State Key Laboratory of Tea Plant Biology and Utilization, Anhui Agricultural University, 130 Changjiang Blvd West, Hefei 230036, China
[b] International Joint Laboratory on Tea Chemistry and Health Effects, Anhui Agricultural University, 130 Changjiang Blvd West, Hefei 230036, China

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ABSTRACT

Tea polyphenols (TP) were emulsified with corn oil and polysorbate 80 by high-pressure homogenization. The oil in water (O/W) TP nanoemulsion had droplet sizes of 99.42 ± 1.25 nm after preparation. The TP nanoemulsion was stable during storage at 4, 25 or 40 °C for 20 days. An *in vitro* simulated digestion assay showed that the bioaccessibility of (−)-epigallocatechin gallate (EGCG) was increased in the nanoemulsion compared to that in aqueous solution, but that the bioaccessibilities of (−)-epigallocatechin (EGC), (−)-epicatechin (EC) and (−)-gallocatechin gallate (GCG) were greatly decreased. Compared with rats fed an aqueous TP solution, rats fed the TP nanoemulsion had significantly lower maximum plasma concentrations (C_{max}) of EGCG and EGC, but the area under the plasma concentration-time curve (AUC_{0-t}) was increased. The data show that use of a nanoemulsion system to deliver tea polyphenols may enhance the absorption of EGCG through controlled release.

1. Introduction

The use of emulsion based delivery systems has gained attention in the food and nutrient industry. An oil-in-water (O/W) colloidal system can increase the dispersibility of a liposoluble bioactive compounds (Qian, Decker, Xiao, & McClements, 2012). For example, nanoemulsion of curcumin increased its stability during gastrointestinal digestion (Sari et al., 2015). An emulsion can also alter the release of the bioactive compound from nano-delivery system, affecting its bioavailability. A nanoemulsion delivery system created a controlled release of curcumin and improved its oral bioavailability (Yu & Huang, 2012). Emulsification can also influence absorption. Hydrophilic bioactive compounds tend to not be absorbed *via* the transcellular route because of their undesirable partition coefficients ($K_{o/w}$). For example, hydrophilic polyphenols that were incorporated into a nanoemulsion system showed improved bioaccessibility and bioavailability (McClements & Rao, 2011; Wang, Wang, & Huang, 2009).

A nanoemulsion is a kinetically stable system containing two immiscible liquids (oil and water) stabilized by a layer of surfactant material that has droplet diameters in the nano range (< 200 nm) (Wang et al., 2009). Nanoemulsions have been used to deliver functional fatty acids, nutrients and some bioactive compounds (Kumar Dey, Ghosh, Ghosh, Koley, & Dhar, 2012). Natural anti-oxidative compounds, such as green tea polyphenols, have been added to nanoemulsion of unsaturated fatty acids or unstable bioactive compounds in order to prevent their oxidation (Luo et al., 2011; Pazos, Gallardo, Torres, & Medina, 2005; Shishikura, Khokhar, & Murray, 2006). An O/W nanoemulsion with tea polyphenols improved the stability and anti-oxidative properties of β-carotene (Wei, Yang, Fan, Yuan, & Gao, 2015).

Anti-oxidant catechins are poorly transported across the intestinal epithelial cells. The use of nanoemulsion has been explored to increase the absorption of catechins (Zhang, Zheng, Chow, & Zuo, 2004; Zhang et al., 2015), suggesting that nanoemulsion can increase the bioaccessibility of catechins compared with non-emulsified catechins (Bhushani, Karthik, & Anandharamakrishnan, 2016). In these studies, Caco-2 cells were used to evaluate catechins bioavailability, but previous studies already indicated that catechins are susceptible to metabolism by intestinal flora (Takagaki & Nanjo, 2009). Actually, most catechins in the gut are metabolized, leaving little to be absorbed in the blood and distributed to organs. Therefore, evaluation of *in vitro* bioaccessibility may not be sufficient to predict the bioavailability of catechins in nanoemulsion delivery systems. *In vivo* pharmacokinetics studies have confirmed that most tea catechins are not absorbed, but are bio-transformed into phase I and phase II metabolites (Baba et al., 2001).

* Corresponding authors at: State Key Laboratory of Tea Plant Biology and Utilization, Anhui Agricultural University, 130 Changjiang Blvd West, Hefei 230036, China.
E-mail addresses: 848358097@qq.com (Y. Peng), 1478895075@qq.com (Q. Meng), 402870413@qq.com (J. Zhou), 837543583@qq.com (B. Chen), 923948380@qq.com (J. Xi), 840521203@qq.com (P. Long), zhli2091@sina.com (L. Zhang), hry@ahau.edu.cn (R. Hou).
[1] These authors Contributed equally to this work.

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Table 1
The stability of tea polyphenols nano-emulsion during the storage at different temperatures (4, 25, 40 °C).

Storage time (day)	Zeta-potential (mV)			Particle size (nm)			pH value		
	4 °C	25 °C	40 °C	4 °C	25 °C	40 °C	4 °C	25 °C	40 °C
0	−16.28 ± 2.01	−23.42 ± 0.57	−24.80 ± 3.09	103.82 ± 0.70	99.42 ± 1.25	99.76 ± 1.32	4.94	4.70	4.44
5	−59.57 ± 4.37	−66.20 ± 5.81	−56.22 ± 2.03	97.68 ± 0.72	98.34 ± 0.78	98.50 ± 1.37	4.83	4.36	4.07
10	−31.88 ± 3.55	−39.70 ± 3.23	−43.08 ± 0.80	96.64 ± 1.08	98.12 ± 0.64	97.22 ± 0.80	4.71	4.17	3.77
15	−27.73 ± 1.30	−51.01 ± 1.45	−43.10 ± 2.19	99.22 ± 0.27	99.44 ± 0.67	101.26 ± 0.61	4.59	3.98	3.5
20	−13.10 ± 0.35	−25.91 ± 0.46	−34.81 ± 0.64	99.22 ± 0.63	98.04 ± 0.93	100.00 ± 1.04	4.63	3.82	3.39

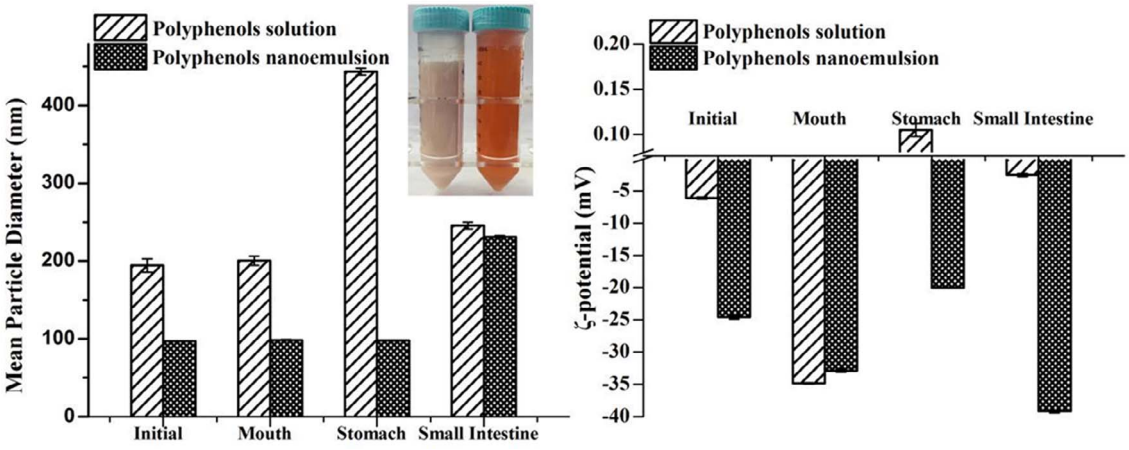

Fig. 1. The particle size (nm) and ζ-potential (mV) of the tea polyphenols nanoemulsion after different steps of *in vitro* simulated digestion.

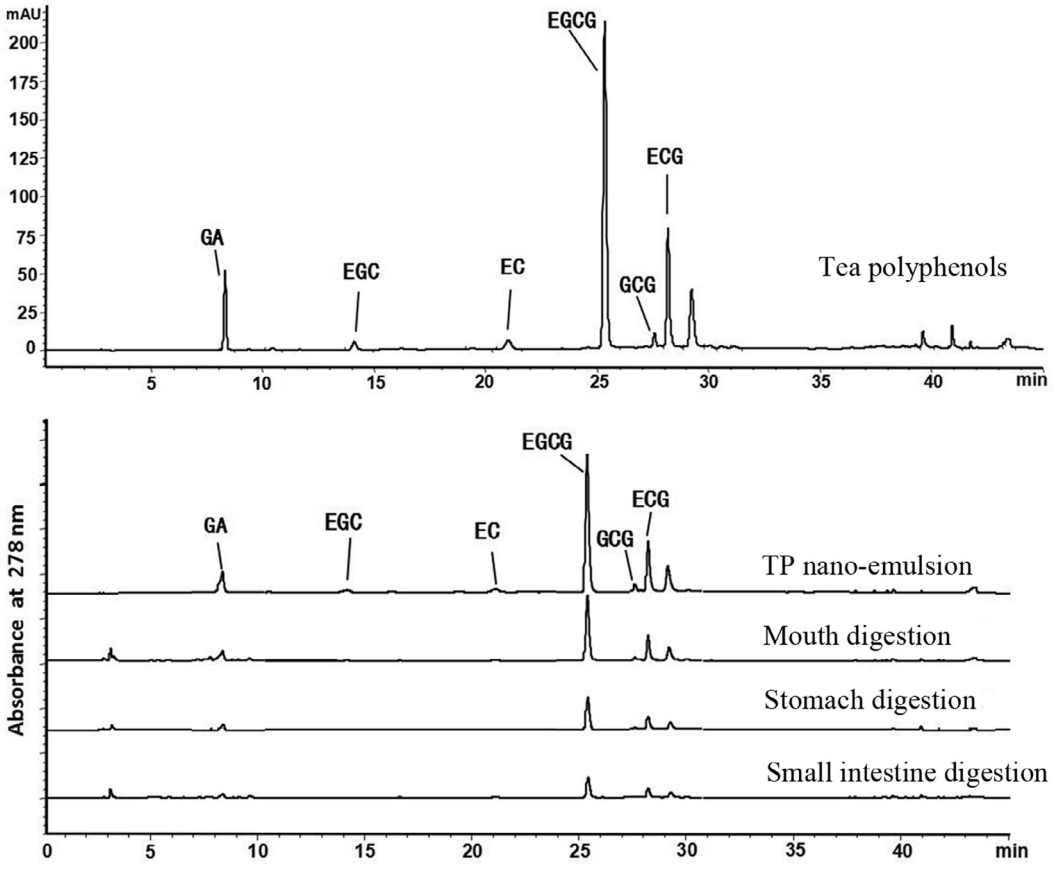

Fig. 2. HPLC of the TP nanoemulsion after different steps of *in vitro* simulated digestion.