RSC Advances

ROYAL SOCIETY OF CHEMISTRY

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Journal Name

ARTICLE

Hyperlipidemia affects the absorption, distribution and excretion of seven catechins of rats following oral administration of tea polyphenols

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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To explore the effects of hyperlipidemia on the pharmacokinetics of tea polyphenols, a comparative pharmacokinetics study of seven catechins between normal and obesity rats was conducted. When rats were orally administrated tea polyphenols (350 mg/kg), the plasma, stomach, small intestine and colon samples of rats were obtained at 5, 30, 120, 360 and 720 min post-administration. The plasma levels of (-)-gallocatechin of obesity rats were significantly less than those of normal rats. During the digestion of tea polyphenols *in vivo*, compared with normal rats, the seven catechins' levels of gastric content and tissue of obesity rats were significantly increased, also the small intestinal tissue levels of (-)-epigallocatechin gallate and (-)-gallocatechin gallate. On the contrary, the colonic tissue levels of (-)-epigallocatechin, (-)-gallocatechin gallate, (-)-gallocatechin and (+)-catechin of obesity rats were significantly decreased compared with normal rats. Furthermore, the fecal excretion of seven catechins of obesity rats was highly increased. To sum up, hyperlipidemia changed the pharmacokinetics of catechins by increasing their distribution in stomach and small intestine, but decreasing their distribution in colon.

Introduction

There have been a large number of researches about the health benefits of tea and tea polyphenols in terms of antioxidant, cancer prevention, lipids lowering and neuro-protective effects.[1-4] So far, the functions of tea have been confirmed by cell experiments and animal studies. As one of the most reported biological activities, tea polyphenols could prevent hyperlipidemia by decreasing the absorption and biosynthesis of lipids, but increasing their catabolism.[5] Furthermore, green tea has shown the promising activities in the prevention of gastro-intestinal cancers, such as gastric, intestinal and colorectal cancers.[6, 7]

After oral administration of tea polyphenols, large intestine and other digestive tracts are the tissues in direct contact with ingested tea polyphenols. On the one hand, it was indicated that a large part of ingested (-)-epigallocatechin gallate (EGCG) and (-)-epicatechin (EC) were distributed in large intestine and esophagus.[8, 9] On the other hand, it was reported that green tea could reduce cox-2 and suppress the formation of colonic preneoplastic lesion and aberrant crypt foci, which is the intermediate step in the development of cancer.[10] Moreover, 0.02-0.32% EGCG as drink fluid showed dose-dependent inhibition on the tumorigenesis of small intestine.[11] The epidemiological studies also provided evidence that drinking green tea may lower the risk of colorectal cancers.[7] It is suggested that pharmacokinetic-pharmacodynamics (PK-PD) modelling in the prevention of gastro-intestinal of tea polyphenols should be worthy of investigation.

It has been verified that galloylated polyphenols such as EGCG and (-)-epicatechin gallate (ECG) were detected in the circulation in the free form, whereas non-galloylated polyphenols circulated mostly in conjugated form.[12] The oral bioavabilitiy of (-)-epigallocatechin (EGC) and EC were 13.7% and 31.2%, which was significantly higher than EGCG.[13] When rats were orally given EGCG (500 mg kg^{-1}), the highest levels of EGCG was detected in the small intestinal mucosa (565 nmol g^{-1}) and colon mucosa (68.6 nmol g^{-1}) of rats. Furthermore, it has been reported that pathological states affected the pharmacokinetics of active compounds,[14, 15] but the widely used tea was less concerned in this topic.

Although there were many reports about the biological activities of tea, the green tea didn't show consistent results on their effects of population-based cohort investigations.[16, 17] It was concluded that the inconsistence was ascribed to the lower blood and tissue levels of tea polyphenols after green tea consumption. The absorption, distribution, metabolism and excretion (ADME) of tea polyphenols *in vivo* is critical to explaining their efficacies. In particular, the distribution of tea polyphenols in targeted tissues should be concerned, such as small intestine and colon. So far, the pharmacokinetics of tea polyphenols was mainly studied using healthy animals or

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human.[13, 18] There were few studies about the effects of physiological and pathological states on the ADME of tea polyphenols.

In this study, we determined the plasma and tissue levels of seven tea catechins in normal and obesity rats following a single-dose administration of tea polyphenols. The information obtained from the present study will provide insights of the absorption, distribution and excretion of catechins in obesity subjects.

Experimental

Chemicals and reagents

EGCG, (+)-catechin (C), EC, ECG, EGC, (-)-gallocatechin gallate (GCG), (-)-gallocatechin (GC) (purity>98%) were purchased from National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China). Methanol and acetonitrile (HPLC-grade) was purchased from Merck (Darmstadt, Germany). HPLC-grade formic acid was obtained from ROE Scientific Inc. (Newark, USA). The tea polyphenols was extracted and refined from the unfermented tea. Tea polyphenols contains seven catechins (54.91% of EGCG, 20.04% of EGC, 11.17% of ECG, 3.37% of EC, 2.13% of GCG, 1.98% GC and 0.51% of C) by the UHPLC-MS determination.

Animal treatment

Thirty male Sprague–Dawley rats (220-250 g) were purchased from the Nanjing Qinglong Experiment Animal Co., Ltd. (Jiangsu province, China). These animals were maintained on a 12 h light-dark cycle (light on from 8:00 to 20:00 h) at ambient temperature (22-24 ℃) and 60% relative humidity. All animal experiments were strictly in accordance with the related guides and ethics regulations and approved by the Institutional Animal Care and Use Committee of Nanjing University of Chinese Medicine. All animals had free access to food and water. The food was removed 12 h before collection of blood samples.

To obtain the hyperlipidemia rats, fifteen rats were given high-fat diet for four weeks according to our published method.[19] The serum lipids analysis showed that the serum levels of lipids of obesity rats (low-density lipoprotein cholesterol, total cholesterol and triglycerides) were significantly increased compared with normal rats (ESI Table 1†). These rats were recruited into pharmacokinetics study as obesity model. In normal and obesity group, rats were orally administered tea polyphenols at the dose of 350 mg kg^{-1}.

After oral administration of tea polyphenols, three rats for each group were sacrificed by inhaling carbon dioxide at 5, 30, 120, 360 and 720 min post-administration, and then 2 mL of blood was collected into heparinized tubes. The blood samples were immediately heparinized and centrifuged at 6000 rpm for 5 min. Supernatant was divided into 0.2 mL aliquots and stored in 1.5 mL polypropylene tubes at -20 ℃ prior to analysis. The digestive tracts were removed and separated as stomach, small intestine and colon according to the anatomical guide. These samples were stored at -80 ℃ until analysis.

Instrument and analytical conditions

The quantitation of catechins in plasma samples was carried out using a TSQ Vantage UHPLC-MS/MS (Thermo Fisher Scientific, USA) including the UltiMate 3000 UHPLC, auto-sampler, column compartment and TSQ mass spectrometer. The analytical method and UHPLC-MS/MS conditions referenced the established method.[20]

Determination of plasma concentration of catechins

To determine the total catechins (free and conjugated from) in plasma, 100 μL rat plasma sample was mixed with 10 μL of a mixture of β-glucuronidase and arylsulfatase (Roche Diagnostics GmbH, Mannheim, Germany), and then incubated at 37 ℃ for 45 min. The reacted mixture was added to 20 μL each of 600 ng/mL I.S. and 20% vitamin C solution (preventing oxidation of catechins) and then vortex-mixed for 1 min according to the published method.[21] The sample was extracted with 1 mL of ethyl acetate by 3 min of vortex-mixing and then centrifuged at 13000 rpm for 10 min at 4 ℃. The upper organic phase was transferred into another tube and evaporated to dryness by an Integrated SpeedVac concentrator system (Thermo Scientific, USA). The residue was dissolved in 100 μL of 20% acetonitrile aqueous solution and vortex-mixed for 1 min. After centrifuging at 17000 rpm for 10 min at 4 ℃, 5 μL of the supernatant was injected into ultra-performance liquid chromatography combined with time-of-flight mass spectrometry (UHPLC-MS/MS) system for analysis.

Determination of catechins in the circulation solution and tissue of digestive tracts (stomach, small intestine and colon)

The weights of main digestive organs (stomach, small intestine and colon) were recorded and listed in ESI Table 2†. Then, they were cut longitudinally and washed extensively. The tissues were immediately frozen in liquid nitrogen. Tissues were stored at −80 °C until use. 0.2 g of each organ tissue was accurately weighed and homogenized with 1 mL of methanol. The homogenate was centrifuged at 6000 rpm for 10 min, and then 100 μL of the supernatant was removed. The supernatant was added into 20 μL of I.S., 20 μL of 20% vitamin C solution and then vortex-mixed for 1 min. The sample was extracted with 1 mL of ethyl acetate by 3 min of vortex-mixing and then centrifuged at 13000 rpm for 10 min at 4 ℃. The upper organic phase was transferred into another tube and evaporated to dryness by an Integrated SpeedVac concentrator system (Thermo Scientific, USA). The residue was dissolved in 100 μL of 20% acetonitrile aqueous solution and vortex-mixed for 1 min. After centrifuging at 17000 rpm for 10 min at 4 ℃, 60 μL of the supernatant was injected into UHPLC-MS/MS system for analysis.

The circulation solutions were collected by wash the content of corresponding digestive tract (stomach, small intestine and colon) with 4 mL of methanol, and subsequently extracted by ultrasonic for 30 min to get homogenate. The homogenate was prepared as the same method above-mentioned. To establish the calibration curves of individual catechin in the tissues of stomach, small intestine and colon, the mixed stock solution was added into untreated tissues of stomach, small intestine and colon, and prepared as the method above-mentioned. The calibration curves for seven catechins were constructed by plotting peak area ratios of the analytes to the concentration homogenate of tissue (ESI Table 3-5†).

Data analysis

Results were analyzed using unpaired Student's t-test. Differences with *p* values less than 0.05 were considered to be significant.

Results and discussion

Time-dependent changes in plasma levels of catechins in rats

The plasma levels of seven catechins of the rats orally administered tea polyphenols (350 mg kg^{-1}) were plotted against time as shown in Fig. 1. The plasma levels of EGCG, EGC, EC, GCG, C and ECG didn't show significant difference between obesity and normal rats, but the maximum plasma concentration(C_{max}) and the area under the curve ($AUC_{(0-t)}$) of GC in obesity rats were significantly decreased compared with normal rats (Table 1).

Table 1 The C_{max} and $AUC_{(0-t)}$ of seven catechins in the tissue and circulation solution of plasma, stomach, small intestine and colon of rats after oral administration of tea polyphenols (350 mg kg^{-1})

Compounds		EGCG		EGC		EC		GCG		GC		C		ECG	
		C_{max}	$AUC_{(0-t)}$	C_{max}	$AUC_{(0-t)}$	C_{max}	$AUC_{(0-t)}$	C_{max}	$AUC_{(0-t)}$	C_{max}	$AUC_{(0-t)}$	C_{max}	$AUC_{(0-t)}$	C_{max}	$AUC_{(0-t)}$
Plasma[a]	Normal	1.547±0744	333.666±115.826	0.524±-0.296	144.101±50.736	0.433±0.166	102.999±30.241	0.039±0.007	9.762±2.668	0.089±0.019	18.314±3.806	0.039±0.019	7.460±1.810	0.425±0.262	95.477±43.704
	Obesity	1.741±0.765	408.312±135.249	0.528±0.290	149.466±57.510	0.397±0.171	105.583±32.192	0.044±0.015	13.889±4.202	0.036±0.012**	6.619±1.891**	0.0326±0.008	7.011±1.488	0.465±0.277	107.743±856.036
Stomach[b]	Normal	88.824±3.209	18885.311±3777.437	39.809±2.509	6172.108±1324.312	10.810±1.218	1727.602±344.607	6.904±1.522	1131.126±224.237	8.218±0.909	1401.121±214.241	1.709±0.340	288.403±70.091	27.126±2.240	6534.711±1602.226
	Obesity	86.115±13.328	32712.524±5194.391*	44.826±2.602	14147.741±3021.911***	13.000±0.800	3961.662±1073.517**	8.221±1.645	2097.826±613.755*	8.609±1.047	2836.483±791.425**	1.907±0.102	576.426±144.917*	30.902±7.114	11210.610±2823.775**
Small intestine	Normal	69.610±20.502	15872.427±4060.509	47.811±6.327	16095.211±3751.439	13.226±3.877	3921.881±1172.639	3.501±1.410	743.508±227.412	8.901±1.533	3277.375±564.723	2.487±0.244	614.411±156.454	29.122±11.776	7689.009±2196.551
	Obesity	91.322±17.753*	22166.102±1426.507*	43.973±9.882	16845.115±4510.542	11.004±4.086	3205.743±1174.933	4.623±1.187*	996.654±369.032*	7.323±2.118	3006.633±862.935	1.522±0.508	447.502±178.421	29.337±7.334	6411.441±2237.576
Colon	Normal	81.451±28.033	30515.33±11760.239	33.101±9.723	16303.124±6449.325	12.435±5.261	5267.821±3005.409	7.224±3.355	2387.121±1236.337	13.446±6.721	4646.214±2131.226	2.977±1.792	1152.922±551.053	36.621±13.911	10816.017±4395.119
	Obesity	87.881±21.432	36890.215±8394.367	22.715±11.323*	9713.227±3427.325**	10.792±5.068	5209.117±2416.432	2.532±0.921**	1256.261±531.014*	4.421±2.210**	2010.002±866.341*	1.281±0.721**	622.9.272±266.614*	27.524±15.003*	10557.257±4638.227

Stomach [c] CS	Normal	22.826±2.871	6045.003±1096.194	6.390±-0.518	1555.382±164.745	3.950±0.382	986.448±229.193	2.096±0.609	634.408±187.841	1.0066±0.0619	333.235±27.373	0.3758±0.05709	135.301±43.901	6.512±2.099	1757.326±505.097
	Obesity	32.320±1.307	8101.872±2136.411	7.7193±2.1263	2428.096±800.683*	3.663±0.081	1163.522±108.226	2.044±0.395	831.615±164.323*	1.4114±0.1109*	547.611±97.044**	0.4118±0.1226	174.380±44.109	9.530±4.258*	3050.639±864.323*
Small intestine CS	Normal	104.724±37.336	51656.759±13968.505	42.332±18.964	18913.027±7267.951	16.462±1.233	7473.449±743.723	13.638±2.326	6020.351±1005.880	7.296±3.206	3520.940±1370.592	1.713±0.426	849.843±213.706	53.030±27.441	23363.775±9188.392
	Obesity	89.683±9.416	41842.212±6620.901	41.674±1.695	17845.366±2838.202	20.131±2.071*	9536.235±1729.860*	11.317±2.598	5888.427±1142.475	7.939±1.118	3403.577±502.691	2.219±0.377	974.829±149.735	55.784±6.800	24200.148±2767.568
Colon CS	Normal	40.033±16.963	17397.096±6457.897	9.590±2.394	4855.868±1378.116	5.669±2.968	1953.010±727.429	4.802±1.792	2259.991±452.335	3.813±1.541	1827.810±439.521	0.575±0.239	238.717±93.689	16.241±3.020	6109.774±1305.248
	Obesity	47.349±6.406	17783.274±3834.217	11.116±1.287	6106.790±824.340	6.023±2.299	2684.723±1021.665	4.041±0.607	1826.910±445.002	3.051±0.759	1622.089±486.267	0.724±0.228	351.927±147.242	17.682±6.918	7845.992±2298.411

[a] the units of C_{max} and $AUC_{(0-t)}$ for plasma catechins were μg mL^{-1} and μg min mL^{-1};

[b] the units of C_{max} and $AUC_{(0-t)}$ for stomach, small intestine and colon tissue's catechins were μg g^{-1} and μg min g^{-1};

[c] the units of C_{max} and $AUC_{(0-t)}$ for stomach, small intestine and colon circulation solution's catechins were μg mL^{-1} and μg min mL^{-1};

CS, circulation solution

*p<0.05, **p<0.01, ***p<0.001, compared with normal rats.

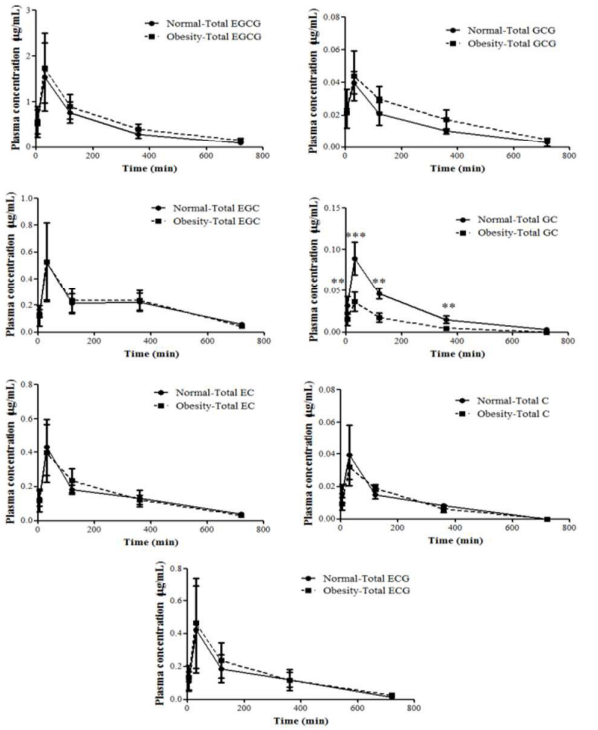

Fig. 1 Time-dependent changes of plasma levels of tea catechins in normal and obesity rats given tea polyphenols solution (350 mg kg^{-1})
**p<0.01, ***p<0.001 compared with normal rats.

Tissue distribution of catechins after oral administration of tea polyphenols

Rats were orally given tea polyphenols at a dose of 350 mg kg^{-1}. In normal and obesity rats, the catechins' levels of gastric content reached the highest value at 120 min, and subsequently decreased. Every catechin showed a similar time-concentration profiling, which suggested that the catechins gallate didn't decompose under the pH condition of gastric juice (ESI Fig. 1†).

The gastric tissue levels of tea polyphenols against time were profiled in Fig. 2. The maximum concentration (C_{max}) of gastric levels of seven catechins didn't exhibit significantly differences between normal and obesity rats, but the $AUC_{(0-t)}$'s of seven catechins in gastric tissue of obesity rats were significantly higher than normal rats. The time-concentration of gastric catechins was profiled in ESI Fig. 1†. As shown in Table 1, it showed the $AUC_{(0-t)}$'s of catechins' levels of gastric content of obesity rats was significantly higher than normal rats, which may result in the increased uptake of catechins in gastric tissue.

Small intestine is the main organ responsible for the metabolism and absorption of catechins *in vivo*. As shown in ESI Fig. 2†, an obvious difference was that the highest catechins' concentrations in small intestinal tract of obesity were detected at 120 min post-administration, which was earlier than normal rats. The C_{max} and $AUC_{(0-t)}$ of EC in small intestinal content of obesity was significantly higher than normal rats. Other catechins didn't show statistical difference between two experimental groups (Table 1).

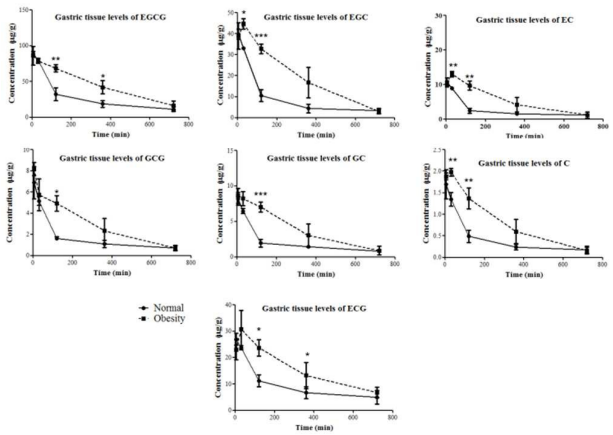

Fig. 2 Time-dependent changes in gastric tissue levels of tea catechins in normal and obesity rats given tea polyphenols solution (350 mg kg^{-1})
*p<0.05, **p<0.01, ***p<0.001 compared with normal rats.

Except for EGCG and GCG, the small intestinal tissue levels of other catechins didn't show significant difference between two groups (Fig. 3). Although the $AUC_{(0-t)}$ of EC in the small intestinal content of obesity rats were higher than normal rats, its distribution in small intestinal tissue were not increased correspondingly. On the other hand, in the obesity rats, the C_{max}'s and $AUC_{(0-t)}$'s of small intestinal tissue levels of EGCG and GCG were significantly increased compared with normal rats (Table 1). These compounds are the main galloylated catechins of tea polyphenols, which have been reported with worse oral bioavabilitiy than non-galloylated catechins. In the present study, these results indicated that the distribution of galloylated catechins was increased in small intestine of obesity rats.

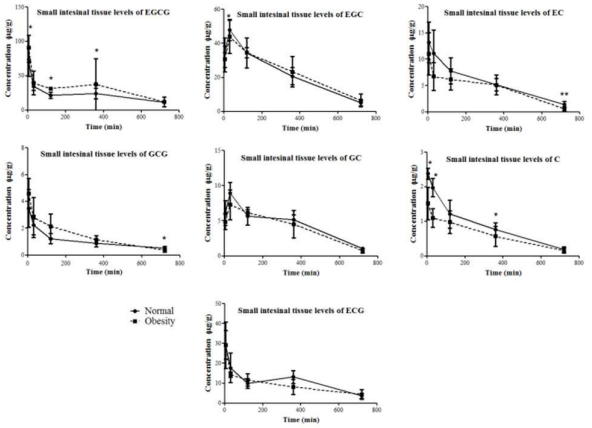

Fig. 3 Time-dependent changes in small intestinal levels of tea catechins in normal and obesity rats given tea polyphenols solution (350 mg kg^{-1})
*p<0.05, **p<0.01, compared with normal rats.

When the tea polyphenols entered into the colonic circulation, the decrease of catechins' levels in colonic content was obviously observed (ESI Fig. 3†). For example, the C_{max} of EGC in small intestinal content of normal rats was 42.332±18.964 μg mL^{-1}, but the C_{max} in colonic content was only 9.590±2.394 μg mL^{-1}. Over half of EGC was metabolized and absorbed in small intestine. The colonic tissue levels of catechins were gradually increased along with the accumulation of catechins in the colonic content.

Colon is the main organ responsible for the microbial metabolism of catechins. The C_{max}'s EGC, GCG, GC, C and ECG in colonic tissue of normal rats were significantly higher than obesity rats (Fig. 4 and Table 1). For example, in the normal rats, the C_{max} of EGC was determined 33.101±9.723 μg g^{-1} in colonic tissue, which was significantly higher than 22.715±11.323 μg g^{-1} of obesity rats. Correspondingly, the $AUC_{(0-t)}$ of EGC was 16303.124±6449.325 μg min g^{-1} in colonic tissue of normal rats, which was also significantly higher than obesity rats (9713.227±3427.325 μg min g^{-1}). The similar results of $AUC_{(0-t)}$'s of GCG, GC and C were observed in the colonic tissue of normal rats. On the other hand, the catechins' levels in the colonic content didn't show significant difference between two groups. These results suggested that distribution of catechins in colonic tissue was not relied on the systemic circulation. The permeability of colonic epithelial cells may be affected after long-term high-fat diet fed, so the uptake of catechins in colonic tissue of obesity rats was decreased compared with normal rats.

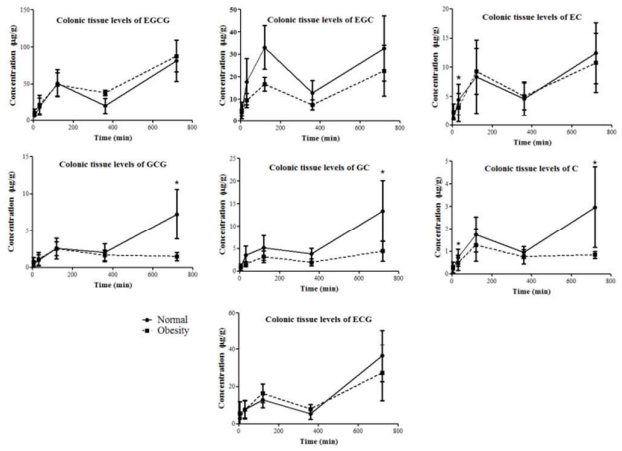

Fig. 4 Time-dependent changes in colonic tissue levels of tea catechins in normal and obesity rats given tea polyphenols solution (350 mg kg^{-1})
*p<0.05 compared with normal rats.

Fecal excretion of tea polyphenols in rats

The fecal excretion of tea catechins was determined and summarized in Table 2. In the obesity rats, the total excreted contents (μg g^{-1}) of EC, EGC, ECG, EGCG, C, GC and GCG from 0-24h were increased compared with normal rats. In the normal rats, the fecal catechins' content only accounted for a small part of oral administered amount (0.516%-1.309%), the excretion ratios of seven catechins of obesity group were increased (1.205-3.375%) significantly compared with normal group as shown in Table 2.

Table 2 Total fecal amount (μg g^{-1} body weight) and excretion ratio (%) of tea catechins in rat after oral administration of tea polyphenols (350 mg kg^{-1})

Compounds		Fecal amount 0-24h (μg g^{-1} body weight)	Excretion ratio 0-24h (%)
EGCG	Normal	2.505±1.430	0.747±0.515
	Obesity	3.118±0.821	1.276±0. 336*
EGC	Normal	0.723±0.445	0.588±0.434
	Obesity	1.075±0.589	1.205±0.661*
EC	Normal	0.106±0.051	0.516±0.317
	Obesity	0.187±0.048*	1.247±0.321*
GCG	Normal	0.171±0.087	1.309±0.844
	Obesity	0.196±0.032	2.065±0.343*
GC	Normal	0.129±0.054	1.068±0.584
	Obesity	0.286±0.117**	3.375±1.391**
C	Normal	0.024±0.010	0.767±0.399
	Obesity	0.036±0.009*	1.594±0.398**
ECG	Normal	0.565±0.333	0.823±0.591
	Obesity	0.740±0.277*	1.488±0.556*

*P<0.05, **P<0.01 compared with normal rats' group.

There have been extensive studies about tea polyphenols' functions. The health benefits of tea have been were verified using various disease models, such as metabolic syndromes and carcinogenesis. Yet the changes of absorption and distribution of tea polyphenols caused by disease model have not been clarified. There wasn't sufficient concerning about the re-evaluation of pharmacokinetics of tea polyphenols in disease models, which may influence their absorption, metabolism, distribution and excretion and then reduce the activities. In the present study, although normal and obesity rats were orally administered the same dose of tea polyphenols, the results showed a significant decrease in the C_{max} and $AUC_{(0-t)}$ of GC in obesity rats. For other catechins, it didn't show statistical differences of absorption between normal and obesity rats. These results demonstrated that hyperlipidemia didn't affect the absorption of main catechins of tea polyphenols, except for GC.

It has been suggested the dominant distribution of EGCG and EC in digestive tracts was attributed to the direct contact or involved in the excretion of tea catechins.[9, 13] In the present study, the catechins' levels in the small intestinal content of obesity rats were similar to normal rats. When carefully comparing the levels of EGCG and GCG in the small intestinal contents of normal and obesity rats, the obesity rats' data didn't show statistical differences. The C_{max} of EGCG and GCG in small intestinal content of obesity rats were even less than normal rats. The most interesting finding of this study is that the small intestinal tissue levels of EGCG and GCG were significantly increased in obesity rats compared with normal rats. These findings indicated that other important pathological factors affected the uptake and distribution of catechins in small intestine. It was reported that obesity rats showed an alteration on tight junction and intestinal permeability. Then, the tissue distribution of tea catechins may be subjected to multiple factors.[22]

By comparing the data of catechins' levels in colon circulation solution and feces, we found that hyperlipidemia significantly influenced the excretion of catechins in rats. As shown in Table 2, before the metabolism by colonic microflora or uptake by large intestine, the concentrations of catechins in colon circulation solution didn't show difference between normal and obesity rats, but after the digestion of tea polyphenols in large intestine, the fecal excretion of catechins was highly increased. It was reported the catechins were metabolized into low molecular weight phenolics by gut floras.[23-27] So, if the high-fat-induced obesity decreases the total bacterial count and increase the relative proportion of *Bacteroidales* and *Clostridiales*, the metabolism of tea catechins may be correspondingly affected.[28] A reasonable reason for this appearance was the metabolism difference of catechins between normal and obesity rats.

Conclusions

The absorption, distribution and excretion of catechins in normal and obesity rats showed differences. Firstly, the absorption of GC was significantly decreased in obesity rats. Secondly, compared with normal rats, the distribution of EGCG and GCG in gastric tissue of obesity was significantly increased,

but the distribution of EGC, GCG, GC and C in colonic tissue was significantly decreased. Thirdly, the fecal excretion of catechins was increased in obesity rats. To sum up, the absorption, metabolism and distribution of tea catechins were different between normal and obesity rats. The distribution of catechins in digestive tract should get much attention, because it may affects their efficacies.

Acknowledgements

Financial support for this research was provided the National Natural Science Foundation of China (31201335), Anhui Provincial Natural Science Foundation (1308085QC51), and Modern Agro-industry Technology Research System in Tea Industry of Chinese Ministry of Agriculture (nycytx-26) and Chang-jiang Scholars and the Innovative Research Team in University (IRT1101).

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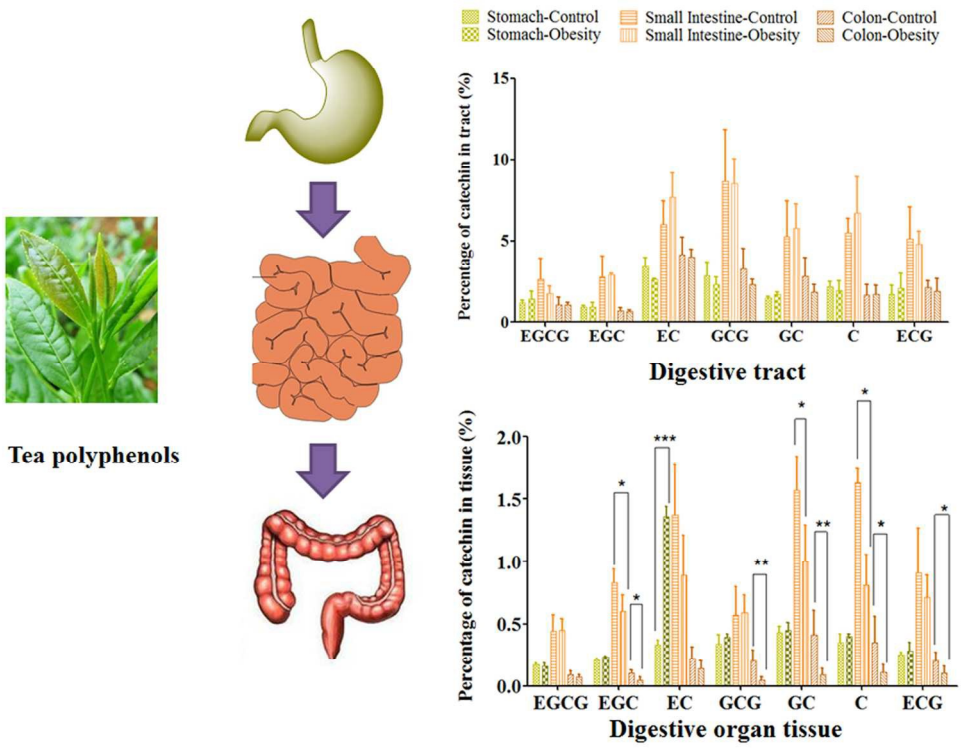

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